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Walden University

College of Health Sciences

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Peter Mgosha

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Walden University
2017

Abstract

Barriers to Switching Patients to Second-Line Antiretroviral

Treatment Among Clinicians in Tanzania

by

Peter Charles Mgosha

MPH, Tumaini University, 2005

ADCM, Kilimanjaro Christian Medical University College, 2003

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

Doctor of Philosophy

Public Health

Walden University

May 2017

Abstract

Poor decision making among clinicians to transferring human immune deficiency virus (HIV) patients into second-line antiretroviral therapy (ART) has led to an increase in morbidity and mortality to people living with HIV (PLHIV). No clear barriers are known for clinicians not switching their patients. This is a descriptive qualitative research aimed to discover obstacles that influence clinicians' decision making to transferring patients into second-line ART despite higher level resistance to first-line ART. The researcher applied a participatory action research framework to solve the identified barriers with clinicians. Using the research questions the researcher explored reasons, perceived barriers and enabling factors for clinicians delay in making decision to transferring HIV patients into second-line ART. In-depth semistructured interviews were conducted with 30 participants. Six thematic areas (a) clinicians' capacity to diagnose treatment failure, (b) laboratory investigations, (c) availability, access, and tolerability to second-line ART, (d) clinicians' perceptions on ARV medicines, (e) clients' readiness for ARV medicines, and (f) adherence and retention to ARV medicines were analysed using STATA. Readiness, adherence and retention to ART, knowledge, competence and experience on ART, lack of viral load testing, and shortage of second-line ART were the common major barriers for clinicians in determining transferring patients into second-line ART. The government of Tanzania should acknowledge and create participation, responsibility, and commitment strategies to reduce the observed barriers. Findings of this study generates knowledge and provide actionable plans to help clinicians easily identify HIV patients who are in need of second-line ART.

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Dedication

My honest dedication to Ms.Asifiwe Wills Temihango (my wife) who indeed worked tirelessly and closely with me to make sure that this extensive passage is coming to an end. I should also devote special thanks to my children (Linda, Liku and Charles) who actually received fair tender love care, as I was working toward finalizing my dissertation.

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Chapter 1: Introduction to the Study

Introduction

Antiretroviral therapy (ART) describes the use of medication to control the replication of human immune deficiency virus (HIV) in HIV-infected individuals (New York State Department of Health AIDS Institute [NYS- DHAI], 2015). The therapy is used to suppress virus replication within the body, restore immunity, prevent death, and improve health of people living with HIV (PLHIV) National AIDS Control Program [NACP], 2015a). About 15 million individuals were receiving ART in 2015 all over the world (World Health Organization [WHO], 2016). Although effective HIV care and treatment programs have been established, some countries struggle to provide ART to HIV-infected individuals (Sidibé, Zuniga, & Montaner, 2014). Among those countries that do have access to ART, such as Tanzania, clinicians often fail to transfer their patients from initial ARV's medications to subsequent second-line ART when first-line treatments lose effectiveness (Ramadhan et al., 2014).

Access to ART does not only mean that all PLHIV and AIDS receive HIV treatment and other determinants for the success of ART provision need to be explored. For example, a clinician's willingness, perception, and capacity in terms of knowledge to provide ART are among of the determinants that may facilitate change from first-line ART to second-line ART when failure is observed. Researchers have recently shifted focus away from the short-term benefits of ART to focus on the long-term difficulties of managing HIV and AIDS (Keiser et al., 2012) while initiating ART to all eligible patients. According to data from the Joint United Nations Programme on HIV and AIDS

(UNAIDS, 2013), about 6% of all patients receiving first-ART in developing nations will need to transfer their patients into second-line ART in near future.

First-line ART is an efficacious and less expensive antiretroviral therapy; it has generic formulations, is often available in fixed dose combination, and does not require a cold chain. In addition, they preserve potent protease inhibitors (PI's) for second-line treatment World Health Organization [WHO], 2013a). First-line ART are drugs given to people who have never been to ART treatment before and if combined with PI's can be used as second-line ART to HIV individuals who clinically, immunologically, or virologically failed to respond on first-line ART. ART regimens commonly require changes, which often involve switches of multiple medications simultaneously. The World Health Organization [WHO], 2013a) suggested that the whole of the ART regimen be changed if the initial first-line ART proves failure.

The second-line ART involves medicines that maintain action over the patient's virus strain and usually comprises a minimum of three active medicines National AIDS Control Program [NACP], 2015a) drawn from at least one nonnucleoside reverse transcriptase inhibitors-protease inhibitors (NACP, 2012). The protease inhibitors are usually combined with two nucleoside reverse transcriptase inhibitors to augment therapeutic index and remove chances of ART resistance (Estill et al., 2013). Second-line ART should be given only when first-line ART has been proven to have failed to suppress an individual HIV virus replication in the human body World Health Organization [WHO], 2013a). The change of that treatment should involve a

combination of drugs whenever the first-line ART is suspected. No change should be made as monotherapy, but rather triple drug combinations should be sought.

The combination of ARV drugs are useful for fighting multiplication of the HIV virus at each stage of its life cycle. These drugs are well-known as highly active antiretroviral therapy (HAART) that reduce the number of HIV copies to individuals' body, preserve individuals' immunity, and prevent multiple HIV-related infections that increases deaths among PLHIV (Laura et al., 2015). They minimize the likelihood of an individual developing drug resistance and thus, improve patients' health (WHO, 2014). It is from this fact that clinicians should realize benefits of using ARV combinations.

According to Barnett et al. (2013), clinicians' knowledge and competence is essential to ART management. Without adequate knowledge, clinicians may lack the confidence to adjust patients' treatment plans when needed. Clinicians are required to initiate ART process in order to prevent morbidity and mortality among PLHIV. A scientific approach to usage of standardized and affordable first-line combinations of ARVs is fundamental to scaling up the provision of ART to patients in need (Hamers et al., 2012). The WHO (2015) recommended that ART be given to adult HIV patients, regardless of their CD4 cell counts (level of white blood cells), as well as gestational and lactating mothers and children under the age of 1 year.

Earlier initiation of ART regardless of CD4 counts reduces individual's ill-health, worsening of the disease with co-infection of other diseases such as tuberculosis; it reduces heterogeneous HIV spread and unwanted or untoward ART drugs complications. Despite WHO recommendations, ART use in Tanzania remains low. Based on the

epidemiological information data from HIV programs, only 2% of HIV people are on second-line ART in Tanzania (National AIDS Control Program, 2013a), although the level of first-line ART resistance is at 14.8% (Kasang et al., 2012). When an individual develops resistance to first-line medicines, it is essential to transfer him or her into second-line ART to maintain therapy benefits.

The high rates of first-line ART resistance in Tanzania indicate that patients are not transferred into second-line treatment timely. To help clinicians understand when to place HIV-infected individuals on first-line ART, and when to transfer them into second-line therapy, the WHO (2015) developed clinical and CD4 criteria to assess patients' eligibility for ART. However, in the absence of clinical and CD4, an individual should not be denied in starting ART. Patients' adherence to ART is another supporting factor for ART treatment initiatives to PLHIV. With good adherence, individuals who begin ART may remain healthy and enjoy long lives.

Poor ART adherence is associated with late initiation of first-line ART (Fox et al., 2012), treatment failure, and drugs resistance (Ramadhan et al., 2014). Fox et al. (2012) claimed that 14% of all patients receiving first-line ART fail virologically within 5 years of their treatment. As the availability of ART continues to grow and the increase use of ART among HIV patients around the world will necessitate use of second-line therapy (Gunda et al., 2017). In order to facilitate and sustain ART treatment adherence to PLHIV, clinicians should provide details for ARV's medication and the significance of strictly staying into ARV's medication. In so doing, adherence to first-line ART will be increased and therefore preventing needless transferring of patients into second-line

ART. VL assessment involves laboratory testing that measures the number of HIV virus particles per milliliter of blood (Barry et al., 2013). These particles are called copies (Cardoso et al., 2014).

Viral load (VL) testing provides information about an individual's health status and indicates how well ART is controlling the virus (Keiser et al., 2013). VL monitoring determines treatment failure and the need for treatment modification or changes (Vanobberghen et al., 2015). Regular VL monitoring can replace the use of clinical and immunologic tests, help avert drug resistance (Sigaloff et al., 2012), and prevent resistance transmission (Phillips et al., 2012). It therefore important to make it available in all HIV health setting. Although VL monitoring of HIV is the most effective way to assess the effectiveness of ART and patients' health, these tests are rarely available in resource-poor countries, such as Tanzania, due to high prices and rigorous necessities for plasma stowage and transportation (Center for Disease Control and Prevention [CDC], 2015).

Poor access to VL monitoring forces clinicians to rely on clinical assessments and immunological tests at making decisions on patients' appropriate treatment, although these assessments are often poor indicators of virological failure (Fox et al., 2012). Viral load monitoring also supports treatment adherence (Hamers et al., 2013), facilitates the reduction of HIV transmission (Cohen et al., 2012), facilitates the early diagnoses of viral load failure among patients on ART, simplifies ART delivery, facilitates task shifting, and reduces the number of care and treatment appointments required for patients (Roberts et al., 2012).

VL monitoring can also prevent unnecessary costs related to switching patients to more expensive second-line ART when viral load failure is not indicated (Phillips et al., 2012). The use of VL monitoring, if efficiently maximized, could reduce the incidence of ART resistance in Tanzania. However, despite the benefits of viral load monitoring, only a few treatment facilities in Tanzania have access to the tests. This is due to their high costs and the fact that the tests cannot be administered in the field as they rely on DNA amplification, a technique that requires bulky laboratory-based equipment and a source of mains electricity (Cairns, 2015). In developed countries, it is standard care to monitor HIV patients who receive ART via VL monitoring to determine when treatment has failed and a switch to second-line therapy is needed (WHO, 2014).

In resource-poor countries such as Tanzania, where access to VL assessment is limited, the WHO (2013a) recommended that treatment failure be assessed by clinical signs or CD4 cell counts. However, clinical symptoms and decreases in CD4 cell counts provide limited detection of virological failure. Consequently, patients with adequate virological suppression are at risk of being incorrectly labeled with treatment failure and undergoing costly and premature switches to second-line therapy. On the other hand, when patients with true first-line ART failure are not switched to second-line therapy, drug resistance mutations that jeopardize future treatment options can occur (WHO, 2013a).

VL testing has the positive predictive value over immunological testing, it only measures what is supposed to measure (accuracy), the test is sensitive and it specifies level of HIV in individual's blood (Jourdain, et al., 2013). Clinicians relying on viral

load results are in better position of making decision on when to shift their patients from first-line to second-line ART (Jourdain, et al., 2013).

Background

The scale-up of ART seems to augment (a) significant number of patients experiencing first-line treatment failure (Chkhartishvili et al., 2014; Johnston et al., 2012), (b) the need for more expensive second-line ART (Bacha, Tilahun, & Worku, 2012), and (c) the development of viral resistance (Ramadhan et al., 2014). Health care professionals monitor patients who start ART aiming to maximize the effective duration of first-line ART and to avoid viral resistance (Roberts et al., 2012). In developed nations, patients on ART have regular VL and immunologic monitoring. However, in resource-poor countries, lack of VL monitoring forces clinicians to depend on inaccurate WHO stages plus immunologic assessments (Vanobberghen et al., 2015).

In the absence of VL monitoring, patients in resource-poor nations will likely continue to experience drug resistance because they will remain on first-line therapy long after the therapy has lost its effectiveness (Cairns, 2015). Drug resistance is inevitable to resource poor countries if viral load test will not be appreciated in HIV care and treatment services. This calls for political will and more budget allocation to priorities viral load monitoring to all patients taking ART. The use of viral load will reduce the shift of patients from first-line to second-line therapy as many of them will be identified early before they fail the first-line ART.

HIV virus is detected in all human body fluids, however, VL in sexual fluids is more closely associated with transmission risk than in blood, although it is not easy to

measure. Having an undetectable viral load is important to HIV patients for a number of reasons. First, undetectable VL indicate the immune system is recovering and growing stronger, which reduces patients' risks of becoming ill due to HIV (Lorenzana et al., 2012). An undetectable VL also reduces patients' risks of developing other serious illnesses, such as heart disease and stroke (WHO, 2013a). Second, having an undetectable viral load reduces an HIV patient's risk of becoming resistant to anti-HIV drugs. Finally, having an undetectable VL reduces a patient's risk of passing HIV on to someone else (WHO, 2015).

If VL is undetectable, then the virus cannot mutate and develop resistance. A constant viral load of <50 copies/ml in the blood is associated with virological benefit (Meintjes et al., 2012). The aim of HIV treatment is to reach undetectable levels of VL. However, just because the level of HIV is too low to be measured does not mean that the virus has disappeared completely from the body; it might still be present in the blood, but at levels too low to detect. VL tests only measure levels of HIV in the blood, which may be different to the viral load in other parts of the body, such as in genital fluids, intestines, or lymph nodes (WHO, 2013a). VL testing is rarely available in resource-poor nations.

For example, Keiser et al. (2012) reported that in Asia and South America, the switch to second-line treatment was likely to happen when patients had higher CD4 cell counts when there was access to VL monitoring than in programs that did not have viral load testing available. VL monitoring has an influence on a clinician's decision to switch patients from first-line to second-line therapy (Keiser et al., 2012) and is fundamental to ART success. Decisions to change ART made based on virological failure, rather than

clinical or immunologic failure alone, results in better patient outcomes (Meintjes et al., 2012).

Access to ART to treat HIV infection and AIDS in resource-poor countries has improved over the past several years (Chkhartishvili et al., 2014). This massive public health operation has been the result of determined political leadership combined with the large-scale production of generic, low-cost antiretroviral drugs. Early reports from resource-poor countries have described high levels of adherence to therapy and short-term virological efficacy rates similar to those observed in developed countries (Chkhartishvili et al., 2014). This has been observed by the WHO (2012), which developed clinical and CD4 criteria to detect ART failure when VL monitoring is not easily available and, or accessed. However, the precision of these alternative assessments are poor in terms of sensitivity and prognostic abilities (Estill et al., 2013).

The positive predictive values for virological failure detection of CD4 and clinical criteria are both below 50% (Estill et al., 2013). Therefore, patients who are assessed with CD4 and clinical criteria often experience delays in transfer to second-line treatment or they are not transferred at all (Estill et al., 2013). Health care professionals are expected to use their clinical opinions, indications of VL, and immunological testing to determine when switch patients from first-line to second-line ART (Costenaro et al., 2014; Jourdain, et al., 2013). The combination of VL monitoring, clinical assessment, and CD4 counts measurement, when properly used, can ensure HIV patients receive appropriate ART (WHO, 2015). For example, Keiser et al. (2012) compared the

outcomes of HIV programs in Southern Africa with and without access to virologic monitoring.

The researchers reported higher mortality rates (25%) in Malawi and Zambia programs, in which patients were only monitored immunologically, compared to South African programs, which used virologic monitoring (Keiser et al., 2012). This implies that, viral load monitoring predicts HIV progression among PLHIV and should be used as a gold standard test to monitor HIV patient outcome and drug therapy. Clinicians' quick responses and decisions regarding ART therapy is important for people living with HIV. Clinicians are responsible for initiating the treatment process through the use of clinical assessment, CD4 count, and analysis of viral load. Without these tools, it is difficult for clinicians to identify patients who are failing first-line ART and need to be switched to second-line therapies (Barnett et al., 2013).

Essentially, clinicians' knowledge and competence is essential to ART management (Barnett et al., 2013). Without adequate knowledge, clinicians may lack the confidence to adjust patients' treatment plans when needed. Clinicians are required to initiate ART process in order to prevent morbidity and mortality among PLHIV. This study explores the clinicians' responsibility of keeping their patients into appropriate HIV treatment.

Problem Statement

A successful ART program requires the following: (a) access and dispensability of ARV medicines (WHO, 2014), (b) clinicians who are able to diagnose HIV treatment failure, (c) access to laboratory investigations, (d) positive perceptions of ART among

clinicians, and (e) ART switching enablers (Ramadhan et al., 2014; Vanobberghen, 2015). Clinicians' inability to monitor and detect failure of first-line ART has led to barriers in managing patients on ART (Bacha, Tilahun, & Worku, 2012; Barnett et al., 2013; Costenaro et al., 2014; Jourdain, et al., 2013). Lack of access to VL monitoring, drug toxicity, tolerability, and high costs related to second-line ART may influence clinicians' decisions to switch patients to second-line therapies (Johnston et al., 2012; Kumarasamy, 2012).

Clinicians' perceptions to second-line ART influence their decisions to switch patients from first- to second-line therapies (Ramadhan et al., 2014; Vanobberghen, 2015). In South African and Asian studies, clinicians perceived that second-line HIV medicines were expensive and not readily available and, therefore, delayed the switching process (South Africa Department of Health, 2014). In addition, the criteria for switching HIV patients to second-line ART are unclear to many clinicians, which further complicates the treatment process (Eholie et al., 2012). Researchers (Barnett, 2013; Sahay, Reddy, & Dhayarkar, 2012) reported that barriers to ART adherence include side-effects, regimen complexity, socio-cultural factors such as complex dosing schedules, alcohol and substance abuse, distance from HIV care and treatment clinics, economic factors, and patient-provider relationships (Ramadhan et al., 2014, p. 2). However, researchers have yet to address clinicians' barriers to transferring patients from first-line to second-line treatment, particularly in Tanzania.

Purpose of Study

This research discovers hurdles among clinicians that cause the delays in transferring patients to second-line ART, despite indications of high levels of resistance to first-line ART (Kasanga et al., 2012). The focus of this narrative study was to provide clinicians with strategies that will help them switch patients from first-line to second-line ART at the earliest appropriate time (Creswell, 2013).

Research Questions

RQ1: What factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

RQ2: What are clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

RQ3: What factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

Theoretical Framework

My study employed a participatory action research (PAR) framework. PAR study involves two different approaches: participatory research and action research (Bergold & Thomas, 2012). When participants and researchers are equal allies, the study focus and outcomes can be significant to a set audience (Faulkner, 2012). PAR is a collaborative process in which researchers and participants are involved in setting study agendas (Ritchie et al., 2014). Participatory research usually entails exploring of research issues and deals with them, while the action research uses the research outcomes to

develop strategies to solve the population issues. Population needs are assessed, and action is taken with an intention of bringing social change through improvement of programs and organizations (Ritchie et al., 2014).

Through PAR, scientists attempt to integrate the three essential features of their efforts: (a) involvement (community life and equal opportunity), (b) success from individual or community integration and their experiences, and (c) proceedings and investigations in terms of idea dependability and knowledge growth (Chevalier & Buckles, 2013). Recently, PAR has expanded from consumer's interest to consumer's engagement in the investigation process, leading to customer-led or customer-controlled investigation (Faulkner, 2012). This type of research empowers participants to become instruments of change (Faulkner, 2012; Ritchie et al., 2014). PAR has made inroads in the field of public health in areas such as disaster relief, community-based rehabilitation, accident prevention, hospital care, and drug prevention (Chevalier & Buckles, 2013).

PAR has been recognized as a problem-solving tool in public health interventions and self-transformation within groups, organizations, and communities. In qualitative methods, researchers can use PAR and inform policy makers and planners to make decisions in solving their existing health problems (Yin, 2014). This study involved participating clinicians as coresearchers in order to explore the perceived perceptions, knowledge, and enablers that influence clinicians' decision to switching patients into second-line ART.

Nature of the Study

I used a narrative qualitative study design (Aschengrau & Seage, 2014) that is best applied in the public health disciplines to enriching policymakers with information and leading them to decision making for community health problems (Aschengrau & Seage, 2014). Qualitative methods allow researchers to explore *how* and *why* issues occur by investigating causes from varying perspectives (Yin, 2014). Qualitative studies are well-suited to PAR approaches (Creswell et al., 2013), making qualitative methodology appropriate for exploring barriers that influence clinicians' decisions to switching patients to second-line ART. Data were collected from 30 clinicians who work in care and treatment clinics in Tanzania to explore barriers that may prevent clinicians from transferring HIV patients to second-line therapy.

Participants were selected via a purposive sampling technique. Data were collected via demographic questionnaire and in-depth interviews. The interview questions were used to explore barriers that precede clinicians' decisions to delay switching adult HIV patients to second-line ART. Interviews were audio recorded and transcribed. Once transcription is complete, interview data were uploaded into Atlas.ti.7.13 to assist with data organization. Data were then classified into themes and categorized for presentation (Stoto, Nelson, & Klaiman, 2012). Further details on the research methodology are provided in Chapter 3 of this dissertation.

Definitions

AIDS: AIDS includes combinations or multiple ill-related signs and symptoms in HIV-infected persons. It is classified as a full HIV infection and is regarded as clinical Stage IV (WHO, 2015).

Antiretroviral-medicines (ARV): Medications used to treat HIV (WHO, 2015).

ART-antiretroviral therapy: The use of substances containing particular strengths to control HIV in infected individuals (NYS- DHAI, 2015).

ART treatment success: A decline of viral load to at least “2 log” from pre-ART baselines; this is achieved after 3 months of treatment initiations or virologically if there is decline of virus to less than 50 particles per ml within 6 months of ART initiation (Kumarasamy et al., 2012).

CD4 counts: Count of white blood cells that fight infection. Generally, white blood cells are the numbers of CD4 cells available in a collected blood specimen. CD4 count facilitates evaluation of the immune system strength (Krucik, 2015).

Clinical failure: In HIV patients, clinical failure refers to episodes or recurrences of infections or tumors, inappropriate growth and development of a child who earlier demonstrated a good prognosis to ART, or poor neurological development in the absence of malnutrition or tuberculosis (Bacha et al., 2012).

Drug resistance: Failure of ART due to transformation of HIV that prevents the medication from destroying the virus. Drug resistance can occur in single and multiple ART (Kasanga et al., 2012).

Drug malfunctioning testing (i.e., the drug resistance testing): Laboratory analysis of drugs used to establish whether patients are experiencing ARV drug failure (Kasanga et al., 2012).

Drug tolerance: A condition in which microorganisms no longer respond to a certain medication, and thus higher dosages are required to attain intended outcomes (National Institute on Drug Abuse [NIDA], 2015).

First-line ART: ART medications consisting of two NRTI reverse and a single NNRTI reverse transcriptase inhibitor (Estill et al., 2013; Keiser et al., 2012).

Highly Active Antiretroviral Therapy (HART): A combination of multiple ARV medications aimed at suppressing HIV replication (WHO, 2015).

HIV: Two types of HIV exist. The first one is HIV-I and the second one is HIV-II. HIV-I is responsible for HIV infections worldwide (WHO, 2015).

HIV replication: The structuring of genetic viruses throughout the infection development within CD4 cells. The function of viral copying is to allow HIV assembly and survival of its kind (Kasanga et al., 2012).

Immunologic failure: A repeat of CD4 cell testing without an increase of CD4 count, despite being on ART. The reduction of an individual's CD4 count while on ART may signify immunological failure (Rawizza et al., 2011; Roberts et al., 2012).

Non-Nucleoside Transcriptase Inhibitor (NNRTI): ARV medicines essential for preventing the initial phase of HIV reproduction (NACP, 2015a).

Nucleoside Reverse Transcriptase Inhibitor (NRTI): ARV medicines essential for preventing transcription of viral RNA to DNA (NACP, 2015a).

Plasma: The clear fluid separated from whole blood, which is collected in ethylenediaminetetraacetic acid (EDTA) tubes (NACP, 2015b).

Protease Inhibitor (PI): ARV medicines required to prevent the replication and maturation of completely contagious viral progeny (NACP, 2015a).

Second-line: Shifting of ARV from the first two NRTI's and a single NNRTI's to a protease inhibitor ART after at least 6 months of follow-up (Estill et al., 2013; Keiser et al., 2012).

Switching treatment: Patients who adjust therapy to a special medicine category; for example, adjustment of nucleoside reverse transcriptase inhibitor to protease inhibitors following clinical or immunological treatment failure (Fox et al., 2012; Kumarasamy et al., 2012).

Treatment adherence: Strictly following ART protocol, including taking the prescribed dosages of medications at the prescribed intervals (Meintjes et al., 2012).

Treatment malfunction: Also known as treatment failure, this describes the presence of new or recurring Stage IV or Definitive Stage III conditions in HIV patients. Treatment failure among patients on ART is indicated when (a) white blood cell counts decline to a pre-ART baseline, (b) when white blood cell counts drop by at least 50%, (c) a patient's constant baseline white blood cell count is less than 100 cells per milliliter, and or (d) a patient has more than 10,000 copies of virus per ml over 6 months of ART initiation (Vanobberghen et al., 2015).

Viral load: Sum of HIV in a specimen of blood. Virologic monitoring serves as a tracking tool to evaluate efficient ART in controlling HIV infection (Fox et al., 2012).

Virological failure: A viral load of over 10,000 copies/ml in the blood while the patient is on ARV for 6 months from the baseline (Vanobberghen et al., 2015).

Viral load testing: The assessment of HIV copies in a specimen of blood from a person living with HIV (NACP, 2015b).

Assumptions

The principal assumption of this study was that participating clinicians do not have the capacity to diagnose treatment failure and possess varied perceptions relating to switching patients to second-line ART (Ramadhan et al., 2014). Enabling factors, such as point of care viral load testing devices, could influence clinicians' decisions to switch patients to second-line ART (Cairns, 2015). It was also assumed that clinicians would have responded openly and honestly to interview questions. Finally, I assumed that the interview protocol effectively addresses the research questions; to ensure this, the protocol was validated by a panel of subject matter experts.

Scope and Delimitations

A study's scope and delimitations describe its boundaries (Bloomberg & Volpe, 2012). The study had included only clinical officers, assistant medical officers, and medical officers to participate in the study. The geographic scope was as well limited because all participants in this study were clinicians working in HIV facilities located in the three municipalities of Dar es Salaam city, Tanzania, including Kinondoni, Ilala, and Temeke. Finally, only participants who had been trained on provision of HIV-ART services and who had at least 1 year of working experience in the field were included in the study.

Limitations

This study was limited to clinicians working in Dar es Salaam city-HIV care and treatment sites alone. Nevertheless, this study did not include laboratory personnel and, therefore, some information relating to the switching of patients to second-line ART may have missed. Data were limited to participants' responses to interview questions, which may have not provided all the possible details. Although many children and youth in Tanzania are infected with HIV, results of this study are limited to physicians dealing with adult patients.

Significance

This study has potentially significant social implications. Findings from this study create a foundation for the recommendation of specific strategies to improve HIV care and treatment across all clinics in Tanzania. As such, generating and sharing knowledge that helps clinicians to identify HIV patients who are in need of a second-line ART. The results of this study if well-utilized, may improve clinical health care services, rather than seeking individuals or health system accountability in rendering HIV care. Findings in this study informs policymakers to critically facilitate development of clinicians training policy that will help the country to have HIV special trainings for these cadres and in particular to proper decision making for HIV management.

As part of the positive social change, the study findings will be used to reduce the barriers that prevent clinicians from providing quality HIV care and treatment services to patients. To translate this study findings, I have already started working closely with senior officials at the Ministry of Health in Tanzania to lead and operationalized them

into an actionable plan. I have planned to disseminate this study findings to all clinics offering HIV services across the country. I have also planned to publish findings of this study and make it accessible to clinicians and other health care provider to allow them review recommendations of this study for better HIV care, treatment, and supports.

Summary

Patients who fail on first-line ART may benefit more from second-line treatment. Keeping patients on failing first-line therapy will not improve their health (WHO, 2014). However, the initiative to move patients to second-line ART at faster rates has been stalled due to (a) clinicians' failure to diagnose first-line treatment failure (Barnett et al., 2013), (b) a lack of access to viral load monitoring, and (c) the use of alternative, inaccurate clinical assessments to determine treatment failure (Keiser et al., 2012; Kumarasamy et al., 2012). No research has been done to assess clinician's perceptions and experiences on switching patients into second-line ART. Thus, a research was needed to understand factors that prevent clinicians from recommending the transfer of adult patients to second-line ART. The following chapter includes a comprehensive analysis and synthesis of the existing body of related research to this study.

Chapter 2: Literature Review

Introduction

This section presents a comprehensive appraisal and analysis to the existing body of literatures interrelated to this study. It begins with a description of the literature search strategy. After that, an analysis of relevant research is presented to contextualize the idea of this study that reveal gaps from previous studies. The chapter closes with a brief summary.

Global initiatives aimed at providing universal access to ART have made these therapies available to a larger number of HIV patients in resource-poor countries (WHO, 2012). In 2015, about 15 million (40%) PLHIV were receiving ART globally, of which 13.5 million received ART in developing countries and of the 13.5 million people, approximately 823 000 were children. So far, improvements to the use of clinical, immunologic, and virologic monitoring among patients receiving first-line therapy are promising (Chkhartishvili et al., 2014). However, many patients who do not respond to first-line therapy need to be moved to second-line therapy (Keiser et al., 2012).

The default first-line ARV drugs for adults and adolescents in Tanzania is the combination of 300 mg of Tenofovir, 150 mg of Lamivudine, and 600 mg of Efavirenz, taken once daily at night. Second-line options for adults and adolescents depend on which first-line ARV drugs are used (NACP, 2015a, p. 131). For patients who are on Tenofovir-based first-line medications, the default second-line choice is Combir, combined with a single separate Amitricitabine drug which is then boosted with ritonavir, a Proteus Inhibitor, or Lopinavir/ritonavir or Atazanavi/ritonavir (WHO, 2015).

These medications comprise of “Tenofovir and Lamivudine or Amitricitabine and Atazanavi/ritonavir or Lopinavir/ritonavir” (NACP, 2012, 2015a, p. 131). The efficacy of ARV drugs depends on the amount of viral load to an individual body (Aberg et al., 2014). The higher viral load in the blood, the poor ARV treatment outcomes (Meintjes et al., 2012). Vanobberghen et al. (2015) exposed that the most common reason that clinicians transfer patients to second-line ART is for viral load monitoring. However, due to poor access to viral load monitoring, particularly in low-income areas, the diagnosis of treatment failure depends largely on clinical and immunological criteria, which are often inaccurate (Kumarasamy et al., 2012).

VL monitoring has an influence on a clinician’s decision to switch patients from first-line to second-line therapy (Keiser et al., 2012) and is fundamental to ART success. Decisions to change ART made based on virological failure, rather than clinical or immunologic failure alone, results in better patient outcomes. Clinicians’ perceptions of second-line ART may also influence their decisions to transfer patients to second-line therapy (Johnston et al., 2012; Ramadhan et al., 2014; Vanobberghen et al, 2015). Understanding clinicians’ decision-making process regarding the transfer of first-line ART to second-line ART may help policymakers and public health practitioners develop strategies to encourage treatment with second-line ART for patients deteriorating on first-line therapy. These strategies may be employed to diagnose treatment failure, explore ART resistance and adherence, and ultimately improve access to second-line ART services in Tanzania.

Literature Search Strategy

Literature for this chapter was located using several databases, including Walden University Library publications, Medline, Science Direct, Google Scholar, PubMed, SAGE, ProQuest, EBSCO, MedScape, EMBASE, and the Cochrane Database of Systematic Reviews. Additional searches were carried out using Google to locate and access editorials, articles, journal topics, institutes, and statistics. Several search terms were employed to locate these studies, including *first-line ART*, *ART resistance*, *HIV/AIDS*, *immunological*, *clinical*, *delay*, *treatment malfunctioning*, *transferring/switching*, *second-line*, *salvage to ARV or ART or antiretroviral substances* and *highly active antiretroviral therapy*, *predictors of antiretroviral therapy*, *clinician's barriers*, and *enablers for active antiretroviral therapy*. Recently published articles and journals were extensively reviewed to minimize the likelihood of missing information resulting from electronic databank indexing lags and other confounding factors.

Theoretical Framework

Participatory research action (PRA) or action research has been defined as a research approach that involves the active participation of stakeholders whose lives are affected by the issue being studied in all phases of research to produce constructive to changes in the community (Chevalier & Buckles, 2013). PRA stems from a philosophy that human beings are capable of analyzing and solving their problems (Yin, 2014). PAR has been discovered by Freire in 1972 and who applied it to persuade underprivileged societies to study and establish the grounds for them being humiliated. Since then, PAR has emerged as an approach that is applied by the researchers to collaboratively work

with societies to achieve planned change through a prioritized action (Freire, 1972).

Bergold and Thomas (2012) suggested using PRA to explore problems in public health, particularly in health care and drugs management. PRA is collaborative in nature because the researchers and participants identify the problem together. Participants and the researcher learn from each other and understand one another's perspectives (Stoto, Nelson, & Klaiman, 2012). PRA discourages a top down approach in which a researcher or health worker comes with ready solutions.

PAR has emerged from constructivism paradigm that allows the researchers to work together with those affected in finding solutions to their problem and it is quite different from positivist paradigm that involves scientific manipulation of variables through laboratory investigations in order to determine the causal effects of a phenomenon. The positivist paradigm is now referred as an old approach as it lacks the following important components when conducting the research (a) it does not identify issues to be addressed in consultation with the study subjects, this is known as the listening phase, (b) it does not help to formulate actions that are to be taken on the prioritized areas, and (c) it does not appear to provide clear opportunities during decision making, including consensus on possible solutions to problems between the researcher and participants (Chevalier & Buckles, 2013).

In this study, I chosen the PAR because I wanted to explore major barriers that may influence clinicians in making decision determination to switching patients failing first-line ART to second-line ART despite higher resistance to first-line ART in Tanzania (Kasang et al., 2012). PAR helped me to work together with clinicians to identify

reasons that makes them delaying the switch of patients to second-line ART and ultimately formulating strategies to eliminate the observed barriers and therefore to improve HIV care and treatment services in Tanzania. Various qualitative studies using the PAR approach have been done to explore the perceptions and feelings of PLHIV on the ART uptake. In Kenya for example, Otieno, Obondo, and Mathai (2012) used PAR to investigate factors influencing nonadherence of ART to patients in relation to alcohol abuse.

With PAR approach both clinicians and patients were able to communicate the importance of ART and identified the associated risks of alcohol consumption and the use of ART. The engagement of patients and clinicians in the research increased ART uptake among PLHIV. Evidence shows that PAR is a good approach in improving HIV treatment adherence and preventing treatment failure and drug resistance to PLHIV (Tangpukdee, 2012). With PAR patients can be engaged with health care providers to reduce HIV risk behaviors and hence, promoting ART uptake (Stoto et al., 2012). A key feature of PAR is the collaborative learning through iterative cycles of action and reflection in which change is generated through new learning and empowering participants (Bradley, Lehmann, & Butler, 2015).

Richter et al., (2015) confirmed use of PAR in six countries Canada, Jamaica, Barbados, Kenya, Uganda and South Africa in which nurses were involved as leaders in building capacity and promoting collaborative action with other health professionals and decision-makers to improve health systems for HIV and AIDS nursing care.

HIV and AIDS

HIV destroys and impairs the function of immune cells. Infected individuals gradually become immune-deficient, which results in an increased susceptibility to a wide range of infections and diseases. The most advanced stage of HIV infection is AIDS, which can take from 2 to 15 years to develop depending on the individual. AIDS is defined by the development of opportunistic infections or other severe clinical manifestations and certain cancers (WHO, 2015). HIV is a leading public health issue across the world, it has caused deaths to 34 million of people so far (Keiser et al., 2013). By 2013 alone, about 1.2 million people died from HIV-related causes (UNAIDS, 2014).

By 2014, about 36.9 million of people were living with HIV and 2.0 million people becoming newly infected in that same year (WHO, 2015). Africa and in particular to Sub-Saharan Africa countries have an estimate of 25.8 million (70%) of people living with HIV globally in which every 12 adults (70%) accounted for the global new HIV infections in 2014 (WHO, 2015). The impacts of HIV and AIDS are on economic degradation in which many people of the reproductive age will continue dying with the disease and probably leaving orphans who will then be subjected to vulnerability state and re-invent the vicious cycle of HIV transmission.

In 2013 about 1.6 million of people were living with HIV and AIDS in Tanzania, and of them 450,000 (30%) were in need of treatment (UNAIDS, 2014). The Tanzania household surveys estimated a 5.1% prevalence of HIV among adults between 15 – 49 years (Ministry of Health and Social Welfare [MOHSW], 2014). Heterosexual intercourse is the main mode of transmission, and women are the most vulnerable

population as compared to men (Tanzania Commission for AIDS [TACAIDS], 2013).

The Tanzanian HIV prevalence accounts for 6% of the total number of PLHIV in the in sub-Saharan Africa, and 4% of all people living with HIV globally (UNAIDS 2014). In 2013, 72,000 people were newly infected with HIV, and 78,000 people died from an AIDS-related illness.

Scaling-up access to antiretroviral treatment has helped Tanzania to minimize the impact the HIV epidemic. Between 2010 and 2013, 5% of all people accessed ART treatment globally (UNAIDS, 2014). The number of people dying from an AIDS-related illness decreased by 44% and the total number of people living with HIV in Tanzania has declined from 7% to 5.1% from 2003/4 to 2011/12 (MOHSW, 2014; UNAIDS, 2014). The severity of HIV epidemic varies with some regions reporting an HIV prevalence of around 1.5% in Manyara and others as high as 14.8%, especially in Njombe (MOHSW, 2014). Overall, the epidemic has remained steady because of ongoing new infections, population growth, and increased access to treatment.

Development and Initiatives on Antiretroviral Treatment Provision

ART has revolutionized the treatment of HIV and has transformed it from a fatal to a medically manageable disease. However, these advancements are not without a cost in terms of drug resistance and side effects (Carter, 2012). The advent of ART in 1996 led to a revolution in the care of patients with HIV and AIDS in the developed world. These treatments have reduced rates of mortality and morbidity and have improved the quality of life of PLHIV (Richardson, Grant, & Zolopa, 2014). The WHO (2012) progress report also confirmed increased survival rate, decreased HIV associated

mortality, and improved quality of life to PLHIV for the fact that, ART makes them free and out of opportunistic illnesses.

The introduction of ARV programs has prevented about 4.2 million deaths in developing nations between 2002–2012 (UNAIDS, 2014). Through supportive supervision and mentorship activities that I conduct semi-annually in HIV care and treatment health facilities, I can see that with ART, life expectancy is increasing among PLHIV. ART has markedly prolonged life of patients with HIV and AIDS. Data from ART programs in South Africa showed that patients in three provinces of the country had increased life expectancy for about 80% for those receiving ART compared to those who are not on ART or started ART in their late stage of HIV infection (South Africa Department of Health, 2014). This finding is supported by the Tanzanian HIV program data that shows a 10% chances of death occurring among PLHIV in the first year of an individual treatment and decreased to around 3% in subsequence years (NACP, 2012).

Antiretroviral Treatment Program

Tanzania began to provide HIV care and treatment services including the provision of ARVs in October 2004. During that period, the national plans, strategies and tools to implement HIV/AIDS interventions were developed. The tools included an assessment of facilities providing care and treatment services, monitoring and evaluation of patients, and overall program monitoring. Training curriculum and materials for health care workers' trainings on comprehensive management of HIV and AIDS were also developed (TACAIDS, 2013). By December 2015, there were 800,431 people current on ART; out of them, 100,848 were children (NACP 2015a).

The Tanzanian government, in collaboration with other stakeholders, simplified ART drug regimens by moving from a singlet type of ART regimen to a fixed-dose combination and phased out toxic drugs such as Stavudine (Vanobberghen et al, 2015). In addition, new guidelines are being issued to increase eligibility and access to ART to sero-discordant couples, all pregnant women living with HIV and key affected populations (WHO, 2016). Standardized national HIV treatment guideline, policy, and strategic frameworks are in use to operationalize management of HIV and AIDS across all HIV programs countrywide.

Tanzania is facing a number of challenges in the scaling-up ART services. HIV prevention care, treatment, and support is reliant on foreign funding, with 95% coming from foreign donors such as PEPFAR, global funds, and other donors (Keiser, et al., , 2013). The support from domestic funds (public revenues collections) is able to support only a few people in need of ART (MOHSW, 2015c). Specifically, there are limited financial resources for first-line and second-line ART and inadequate patient monitoring systems for PLHIV (MOHSW, 2014).

There is also a weak supply chain management system in terms of laboratory investigation before and when patients are on ART, and there is poor ARV drug management in which drug stock-outs occurs more often (MOHSW, 2014). ARV drugs are prescribed free of charge to all eligible HIV patients in 1,700 health facilities across the country (Kasang et al., 2012; NACP 2015a). Being working both with TACAIDS and NACP of the MOHSW, I realized that the scaling-up of HIV services do not progress

well, and or match with the national HIV response plans and strategies. This is due the fact that there are limited resources to make these services viable.

The provision of free ART has been practiced in several middle- and lower-income countries. This has been a national strategy to reduce mortality among HIV-infected patients (Bhatta et al., 2013). In addition to the free of cost ART, HIV-infected patients are offered care packages that include clinical follow-up monitoring; TB screening and Isoniazid preventive therapy; community- and home-based care (CHBC), which includes the primary care of patients by trained CHBC workers at homes and community settings aiming at positive living, reducing stigma, and discrimination and supporting sanitation and hygiene; continuity; and adherence to ART. Moreover, medical, nutritional, psychosocial, and legal support is provided by CHBC; in addition, financial support is provided to newly enrolled patients by community care centers in nearby ART health facilities (National Centre for AIDS and STD Control [NCASC], 2012). With the knowledge I have on HIV care and treatment, the continued provision of ART and supportive services to PLHIV contributes to the retention of people currently on ART in Tanzania.

Antiretroviral Drugs

ARV drugs help to stop HIV if used early. These drugs have a primary goal of achieving a maximal and durable suppression of viral load to < 50 copies/uL. Specifically, ARV drugs repairs and protects immunity of PLHIV. It also reduces multiple illnesses and deaths related to HIV infection among PLHIV (Meintjes et al., 2014). The secondary goals of ARV's are to prevent new HIV infection among

individuals in the community through early HIV testing and counseling where many people know their HIV status and prevent themselves from acquiring the disease through practicing safer sex and therefore, reducing HIV transmission among discordant couples, reducing risks of HIV transmission from mother to child, and reducing the pool of individuals who are infectious to the community (NACP, 2015a). With a vast experience that I have through working in various HIV interventions such as ART program, PMTCT and TB/HIV, I have noted that PLHIV and who are early initiated on ART, looks healthier compared to HIV patients who are yet to start ARV medications.

The currently existing and commercially available ARV fall into the following four main categories: (a) the “nucleoside reverse transcriptase inhibitors” (NRTIs), (b) the “non-nucleoside reverse transcriptase inhibitors” (NNRTIs), (c) “protease inhibitors (PIs)”, and (d) “integrase, also termed as Integrase strand transfer inhibitors (INSTIs) and the entry inhibitors” (Meintjes et al., 2014, p.2). The nucleic acid analogues of NRTIs and NNRTIs mimic the normal building blocks of DNA, preventing the transcription of viral RNA to DNA (Keiser et al., 2013). Specifically, the NNRTIs alter the conformation of the catalytic site of reverse transcriptase and directly inhibit its action, whereby PIs inhibit the final maturation stages of HIV replication, resulting in the formation of non-infective viral particles (WHO, 2013b).

The integrase inhibitors inhibit viral integration and prevent the transfer of proviral DNA strands into the host chromosomal DNA (Meintjes et al., 2012). The entry inhibitors are entry inhibitors of the virus getting into the RNA; they usually bind to viral gp41 or gp120 or host cell CD4+ or chemokine (CCR5) receptors (Meintjes et al., 2014).

ART involves taking a combination of HIV drugs that prevent HIV from multiplying (making copies of itself), which reduces the amount of HIV to an individual body (Kasang et al., 2012). I have seen that, individuals adhering to ARV have a strong immune system that gives them a chance to recover and fight off infections.

The drugs that are available in Tanzania under NRTIs include, Zidovudine (AZT), Lamivudine (3TC), Amitricitabine (FTC) and Abacavir (ABC), and Tenofovir (TDF). The NNRTIs are Nevirapine (NVP) and Efavirenz (EFV), and the PIs are Atazanavir (ATV), Lopinavir (LPV), and Ritonavir normally used as a booster PIs drugs. Currently, there are no (InSTIs) or entry inhibitors available in Tanzania (Vanobberghen et al., 2015). And so, the choice of HIV drugs depends much on individual's needs and the national HIV treatment guideline.

First-Line Drugs

The effectiveness of first-line drugs, commonly known as ART has improved markedly over the years and especially in Sub-Saharan African countries. First-line ARVs are drugs given to patients who have never received ARV treatment before (WHO, 2015). Triple combination therapy has been in use for the past decades globally (Tsague & Abrams, 2014). Currently, the preferred first regimen triple therapy in Tanzania is two NRTI + one NNRTI or two NRTI + one PI or three NRTIs (NACP, 2015a). These drugs include TDF+3TC+EFV, TDF+3TC+NVP, TDF+FTC+EFV, TDF+FTC +NVP, AZT+3TC+EFV, and AZT+3TC+NVP (NACP, 2015a). The default first-line regimen comprises Tenofovir/Lamivudine/Efavirenz and are in a fixed dose combination (NACP, 2015a).

Alternatively, AZT+3TC+NVP can be given as a first-line regimen when Efavirenz has an interaction with other medications or in mental illness complications (WHO, 2013a). The Tanzania national HIV and AIDS treatment guideline emphasize rational use of first-line ART for PLIHIV in order to prevent drug resistance.

Second-Line Drugs

Options for second-line therapy after a failure to the NNRTI, generally involve the switch from the first-line NNRTI to a PI and alternate NRTIs. Second-line ART are drugs given to HIV patients who clinically, immunologically, and or virologically failed to respond on first-line ART (WHO, 2015). The second-line medicines in Tanzania consist of “ATV/r or LPV/r +TDF/FTC; ATV/r or LPV/r + AZT/3TC and ATV/r or LPV/r + ABC+3TC” (NACP, 2015a, p.40). Second-line ART helps individuals achieves durable viral suppression, prevents disease progression and reducing long-term AIDS-related mortality in high HIV prevalence countries such as Tanzania where there is no access to third-line ART regimens.

Criteria for Antiretroviral Therapy Initiations

ART brings a complex series of choices: when to initiate therapy, what regimen to use, which medicines to use within each class, when to modify treatment, and which options of medicines to use in different needs (WHO, 2013a). According to national HIV and AIDS treatment guidelines in Tanzania, 2015, the criteria for initiating ART for adults and adolescents are CD4 count < 500cells/mm³ regardless of WHO clinical stage, pregnant and breastfeeding women, children, individuals with TB and HIV co infection, HIV individuals co infected with Hepatitis B virus and for vulnerable individuals such as

intravenous drug users , men having anal sexual intercourse among themselves ,detainees as well as serodiscordant couples irrespective of CD4 cell count (NACP, 2015a). Without ART, most HIV-infected individuals will eventually develop progressive immunodeficiency and leading to premature death and so, ART is given to PLHIV in order to prolong their life.

Changing Antiretroviral Therapy

Clinicians need to continually assess patients for treatment outcomes while on HIV therapy. They should be able to change or modify ART once negative outcomes are observed to patients. Treatment change may be either due to the risk of acute toxicity, long-term toxicity, treatment failure, poor adherence, a desire for pregnancy, co morbidity with other chronic diseases, or stock-out of drugs (WHO, 2015). The strategy to switch ART depends on the reason for change, the amount of previous ART experience, and the available treatment options (Jima et al., 2013). For example, when patients develop an adverse effect to a drug, effective treatment may be accomplished by substituting another agent for the offending drug in the regimen (WHO, 2013a).

Patients who have experienced toxicities, treatment failure, and drug resistance during past regimens may require a switch to a new treatment regimen (Jima et al., 2013). Patients should be evaluated after a treatment switch to assess for potential concerns with the new regimen and medication tolerance, and targeted laboratory testing should be conducted (Vallabhaneni et al., 2015). “For example, if lipid abnormalities are present, and/or are a reason for the ARV change or are a concern with the new regimen, fasting cholesterol subsets and triglycerides should be assessed within 3 months after the change

in therapy” (Da Cunha et al., 2015, p.25). If any specific complaints, laboratory abnormalities, or viral rebound are absent at the 3 months’ visit, the patient may resume on a regularly scheduled basis (WHO, 2013a). I may then conclude that whether to change or modifying ART due to poor virologic suppression patients’ assessments should be done.

Clinicians believe that any changes in clinical status of a patient on ART could be an indication for treatment interaction and therefore, a need for ART modifications. Medications used to treat comorbid illnesses often interact with ARV agents (Fox et al., 2012). A prime example is the interaction of rifampin with both NNRTIs and PIs. This interaction may be avoided by the substitution of EFV for NVP, perhaps by dose adjustment of EFV, or by the substitution of rifabutin for rifampin in the case of PIs (NACP, 2012). Other important drug interactions include statins with PIs, oral contraceptives with NNRTIs or PIs, and ergot derivatives with PIs (CDC, 2016). Prevention of drugs interacting to ART is important to maximize treatment efficacy and thereby improving an individual health. Programs implementing HIV care and treatment services recommends a routine monitoring of people taking ART to see if whether they are adhering to treatment.

The Tanzanian Ministry of Health and Social Welfare (2015) emphasize that, first-line treatment failure should not only be sought when there is drug resistance. However, issues like (a) untimely dosing, (b) nonadherence, and (c) evidence of malabsorption should as well be assessed to individual patients. It is important to identify the causes of first-line treatment failure and correct them appropriately (NACP,

2015a). Treatment failure based on the WHO set criteria necessitate a change of first-line ART to second-line ART after ruling out nonadherence (NACP, 2015a). The new regimen should comprise of at least two effective drugs (WHO, 2013a).

Patients needing second-line ART should psychologically be prepared for treatment readiness and provided with adherence counselling (Meintjes et al., 2014). Poor adherence reminds me on the importance of providing adherence trainings to all clinicians working in care and treatment settings in which ART is administrated, and indicates that strengthening education and counseling among HIV patients should be a priority for treatment failure prevention in Tanzania. Improved ART adherence mentorship for health care providers is also important, especially among those with limited resources to VL and immunological tests.

ART changes due to toxicity have been associated with many factors demographic characteristics such as female sex, age, ethnicity, genetics, HIV disease status, type of ART, and co morbidities (Mihanović et al., 2013). Toxicity-related ART changes are most frequent within the first 3 months of ART (Kumarasamy et al., 2012). Aside from ART toxicity, treatment failure and pregnancy have been associated with treatment changes (Bayou et al., 2014). In addition to toxicity, anemia and rash also accounts for ARV treatment changes (Jima et al., 2013). Mekonnen and Molla (2014) reported that treatment modification practice is now increasing among clinicians not only due to toxicity, co-morbidity, pregnancy, treatment failure, anemia, and rash but also due to peripheral neuropathy.

ART treatment modification has been important for PLHIV due to the positive impact they have to individuals (Kumarasamy et al., 2012). For example, people who desires pregnant usually undergoes a treatment modification in order to maintain the fetus wellbeing especially if NVP drug is among of the combination in the first-line ART (Mulugeta & Chane, 2012). NVP is prohibited in pregnancy as it increases risk of hepatitis to pregnant women, especially in women with higher CD4 counts (Meintjes et al., 2014). Unlike pregnant and adverse drug reactions, other reasons for ART substitution include the co morbidities such as tuberculosis (Sandeep et al., 2014) and the cost of ARV (Woldemedhin, & Wabe, 2012). ART treatment modifications have been a critical component for HIV and AIDS management and will most likely continue to be important for the society wellbeing, particularly to PLHIV.

Monitoring Patients on First-line Drugs.

Monitoring of people on first-line treatment is one of the important parameter to prevent unnecessary switch of second-line ART (Kumarasamy et al., 2012). A good indicator for the efficacy of first-line ART is associated with an increased weight and reduced ill-health conditions that are related with HIV infection (Keiser et al., 2012). In this case, patients should regularly be taken their history and physical examination in each clinic visits (Laurent et al., 2012). Appearance or persistence of opportunistic infections, or lack of weight gain can indicate treatment failure hence, should require further evaluation to determine fulfillment of criteria for treatment failure (Aberg et al., 2014). This is possible if all clinicians maintain a culture of performing both physical and systematic examination for their patients during each visit at care and treatment

health facilities. Clinicians should also keep in mind that clinical criteria alone do not grantee switching of individuals into second-line ART, however, other switching parameters needs to be considered as well.

Immunological Monitoring

Modeling studies suggest that CD4 cell count becomes one of the criteria to determine the eligibility for initiation and defining immunological treatment failure (Krucik, 2015). Although initiation of ART in patients with TB, HBV, key populations, pregnant and lactating women, HIV positive partners in discordant relationships, and in advanced HIV disease is done irrespective of CD4 count level, it is advised to determine baseline CD4 count in these individuals to monitor immunological response (Ferreyra et al., 2012). A rise in CD4 count indicates effective ARV treatment and that, CD4 count should be repeated semi-annually and at any time if need be (Ferreyra et al., 2012). Immunological testing generally reflects ART monitoring, hence emphasizing the importance of a confirmatory CD4 cell count is typically what clinicians are required to prescribe to their patients before and after ART initiation.

Viral Load Laboratory Monitoring

VL testing has been referred as the gold standard for monitoring ARV drugs responses (Vallabhaneni et al., 2013). This is the preferred approach compared to immunological and clinical monitoring and for the reason that it has higher sensitivity and specificity (Aberg et al., 2014). The use of VL monitoring improves patient's clinical outcomes and preserves second line options (Ford et al., 2012). Where facilities are available, targeted rather than routine VL testing is recommended (Laurent et

al.,2012). Targeted VL testing is only done when treatment failure is suspected (Keiser et al., 2012). Having a VL <50 copies/ml implies treatment success (Vallabhaneni et al., 2012), and in resource-poor countries such as Tanzania, where sensitivity of clinico-immunological is commonly low, VL could be potentially used to detect treatment failure and for decision making on second-line switching practices.

Monitoring Patients on Second-Line Drugs

The outcomes of second-line therapy have been satisfactory and largely consistent across different settings (AJose et al., 2012). This findings emphasizes on the following laboratory tests to be undertaken in monitoring patients on second line drugs (a) CD4 at baseline and 6-monthly, (b) full blood count before treatment, followed with a 3 months consecutive monitoring, (c) performing a fasting cholesterol and triglyceride before treatment, then 6 months later and thereafter 12 months later (d), conducting a liver function tests, (ALT) every after 6 months, (e) conducting fasting blood sugar once in a year (f) conducting urinalysis before treatment and every after 3 months, and (g) conducting serum creatinine before treatment and every after 12 months (WHO, 2015). Monitoring of second-line ART aims to minimize morbidity and mortality among persons on ART and this should be reinforced to all sites offering ART services in Tanzania.

Antiretroviral Medicines Switching Protocol in Tanzania

To contextualize the discussion on first- and second-line ART, it is appropriate to begin with an explanation of the ARV medications that comprise ART. If patients were on Zidovudine as a first-line and were never treated with Tenofovir-based ARV

medicines, the default second-line ARV medication of choice is Tenofovir-based ARV medicines (NACP, 2015a). For patients who started with Tenofovir as a first-line medicine, probably due to Zidovudine intolerance, the default second-line options are Abacavir combined with Lamivudine plus ritonavir boosted Proteus Inhibitors or Atazanavir/ritonavir or Lopinavir/ ritonavir (Wang et al., 2015). The default first-line medication for children under the age of three is Abacavir combined with Lamivudine plus Lopinavir/ ritonavir tablets (Thompson et al., 2012). A substitute to this is Zidovudine combined to Lamivudine plus Lopinavir/ritonavir.

In the event that Lopinavir/ritonavir is not available, Nevirapine is used as an alternative and is given as Zidovudine combined to Lamivudine plus Nevirapine (NACP, 2012). A combination of these drugs is widely used in almost all care and treatment sites in Tanzania where I can see significant improvement of patient's life. Children over the age of three are given Abacavir/Lamivudine plus Efavirenz. For those failing first-line NRTI's ARV medicines, a boosted Proteus Inhibitor combined with two Nucleoside Reverse Transcriptase Inhibitors will be an option for second-line medication (WHO, 2013a). Ideally, a Lopinavir/ritonavir boosted Proteus Inhibitor is the best option for second-line ART (NACP, 2012). When there is first-line treatment resistance to kids over 3 years, NNRTI plus two NRTIs is the best choice for them. Efavirenz is an ideal NNRTI (NACP, 2012; NACP, 2015a, WHO, 2015), to maximally suppressing viremia into their body.

After failure of a first-line based ARV medicines, Abacavir or Tenofovir combined with Lamivudine is the best choice of ART for second-line treatment (WHO,

2013a). When there is failure of a first-line based ARV medication containing Zidovudine or Stavudine combined with Lamivudine, the ideal NRTI choice for second line ART is Abacavir or Tenofovir combined with Lamivudine (NACP, 2015a). As per the national HIV treatment guidelines detailed have been stipulated to help clinicians prepare treatment plans for their patients and for deciding when to switch patients from first- to second-line therapy. Accordingly, this chapter is organized into six thematic sections including; (a) capacity of clinicians to diagnose treatment failure, (b) laboratory investigations, (c) tolerability and cost for ARV drugs, (d) clinicians' perceptions on ARV drugs, (e) burnout/stress, and (f) adherence and retention to ARV drugs.

Thematic Sections

capacity of clinicians to diagnose treatment failure

Researchers have found that clinicians' knowledge and competence is essential to the timely switch of HIV patients to second-line ART (Barnett et al., 2013). Without adequate knowledge, clinicians may lack the confidence to adjust patients' treatment plans when needed (Ramadhan et al., 2014). One of the problems clinicians face with diagnosing first-line treatment failure is related to WHO recommended stages of HIV, which relies on routine clinical assessments (Jourdain et al., 2013). For example, during their study in Mozambique and Uganda, Costenaro et al., (2014) found that reduced capacity to monitor and detect the failure of first-line ART was a key reason that clinicians delayed switching patients to second-line therapy.

Similarly, researchers in Ethiopia found that most first-line ART failures were detected late; thus, patients who needed second-line ART were not switched in a timely

manner (Bacha et al., 2012). The lack of access to viral load monitoring requires clinicians to depend on clinical WHO criteria to detect first-line failure, which often results in poor treatment outcomes and drug resistance (Bacha et al., 2012; Robert et al., 2012), and therefore, progression of HIV to AIDS related illness and complications. Other studies indicate that, clinicians' relationships with patients and workloads influence health service delivery (Jourdain et al., 2013). For example, researchers in India found that clinicians did not have adequate time to provide ART patients with adherence counseling due to other responsibilities, such as taking patients' histories and conducting physical examinations or laboratory investigations (Joglekar et al., 2012). In addition, physicians were unable to detect treatment failure and adjust patients' treatment plans in a timely manner (Levison et al., 2012). Patients and clinicians' rapport that is coupled with less workload can influence smooth managements of PLHIV especially where there is higher prevalence of HIV such as in Tanzania.

laboratory investigations

Poor access to laboratory infrastructures is another hindrance to effective HIV treatment in most Sub-Saharan nations in Africa (Ramadhan et al., 2014). Consequently, viral load monitoring is inaccessible to many clinicians in this region (Adeyinka & Ogunniyi, 2012). Private donors and governments have been unwilling to prioritize clinicians' access to viral load monitoring due to high costs of the tests (Cairns, 2015). The high price of these assessments may be related to supply and demand; as more patients experience first-line ART failure, there is an increased need to detect such failure in order to move those patients to second-line therapy (Cardoso et al., 2014).

The cost of not detecting first-line treatment failure increases mortality rates (Gspaner et al., 2012), to PLHIV. In South Africa, where routine VL monitoring occurs, the rate of switching patients to second-line is higher. Thus, mortality rates are lower in South Africa than in neighboring Zambia and Malawi, where viral load monitoring is not a routine part of ART therapy and not widely available to all health facilities offering ART (Keiser et al., 2012). Costing studies indicate that VL monitoring is not cost effective compared to CD4 monitoring (Kahn et al., 2012), or clinical monitoring alone. To date, however, these studies have only considered the value of adding VL monitoring to clinical and immunological monitoring (Ford, Roberts, & Calmy, 2012).

Studies conducted on ART in resource-poor countries with VL monitoring and those having no VL monitoring in Africa, Asia, and South America indicated that switching patients to second-line ART often occurred earlier and at higher CD4 cell counts in ART programs with VL monitoring compared to programs without viral load monitoring (Chkhartishvili et al., 2014). The lack of VL monitoring if not well addressed will continue to create a meager patients' enrollments to second-line ART especially in developing countries including Tanzania. Concerns exist regarding the use of clinical and immunologic monitoring to detect treatment failure. Multiple studies, including a systematic review conducted to inform the development of the 2013 WHO guidelines, highlighted poor predictive values of the 2010 WHO clinical and immunologic criteria (Chang, Harris, & Humphreys, 2012).

An exclusively use of clinical and immunologic testing contributes to delays in switching of patients to second-line ART (Ramadhan et al., 2014). In addition, these

assessments often lead to misdiagnosis of treatment failure that leads to unnecessary switching (Tucker et al., 2014). Delayed switching increases the risk of drug resistance (Aghokeng et al., 2012), and subsequently, creates higher VL (Adetunji et al., 2013). On the other hand, early or unnecessary switching can reduce the effectiveness of second-line treatment and increase cost burdens (Long et al., 2012; Tucker et al., 2014). Support for simpler, more affordable technologies such as the use of point of care VL monitoring devices could reduce rates of resistance to ART (Hamers et al., 2012).

tolerability and cost to ARV drugs.

tolerability

The emerging resistance to first-line ART intensifies the use of pricey and less tolerable second-line medicines (Hosseinipour et al., 2013). Hence, it is essential to identify and address factors associated with the increased probability of first-line ART failure (Bacha et al., 2012). Meintjes and his colleagues (2014) described that medications used in second-line ART are rarely tolerated by patients, due to toxicity such as hypersensitivity reaction; kidney failure; progressive neuropathy and gastrointestinal complaints (Ciaffi et al., 2015). Toxicities due to medication often prompts poor adherence to ART among PLHIV. Findings from previous studies has revealed that patients on second-line ART, some fail relatively quickly; an estimated 33%–40% of patients receiving second-line ART are failing (Van Zyl, 2012), potentially due to medication nonadherence (Sigaloff et al, 2012).

Due to the apparent high genetic barrier to resistance mutations in patients receiving boosted PIs (Vanobberghen et al., 2015), most patients failing PI-based second-

line regimens do not have PI resistance mutations, suggesting that nonadherence may be the main reason for treatment failure (Murphy et al., 2012). Moreover, compared with patients who switched to second-line ART due to accumulated resistant viruses, those who switched with wild type viruses were less likely to achieve viral suppression (Lorenzana et al., 2012). This observation may also suggest that medication nonadherence is responsible for treatment failure among patients switched into second-line ART (Hansana et al., 2013). Because success of second-line ART depends on high levels of adherence, these observations imply that adherence on first-line may be an important indicator of adherence to second-line ART (Murphy et al., 2012). If true, targeted interventions could be implemented for these patients before switching to second-line therapy and may improve patient outcomes.

cost analysis for antiretroviral drugs

Evidence shows that declining prices for ARV medicines in recent years have made expanding treatment programs more affordable (Hosseini-pour et al., 2013). Prices have declined despite the wider adoption of more expensive TDF-based regimens, which can be attributed to the continued scaling up of treatment programs, greater predictability of demand and increased competition among manufacturers (Estill et al., 2016). For example, the cost of the fixed-dose combination of the WHO recommended. First-line regimen of TDF + FTC + EFV was US\$ 186 per person per year in 2012, whereas a two-pill regimen using the same drugs costs only US\$ 112 (WHO, 2013b). This implies that prices for ART are escalating making difficulties for poor countries to maintain their patients into the recommended first-line therapy.

The costs of first-line ART is much higher in middle-income countries such as Brazil and the Russian Federation, for example, pay more than US\$ 1000 per person per year for the WHO recommended first-line TDF + (3TC or FTC) + EFV (AVERT, 2015). The prices of second-line regimens also declined substantially between 2010 and 2012, but the median prices remained higher than for first-line regimens (Estill et al., 2016). The pricing evidence has been observed from a South African study that revealed that the cost of second-line treatment doubles first-line ART price in a year (WHO, 2013b). It is anticipated that the use of second-line ART will increase in the near future due increase of patients needing second-line ART (Long et al., 2011), while prices for second-line ART are non-predictable for patients to afford.

In 2012 alone, the median reported cost of the most commonly used second-line regimen 3TC + AZT + LPV/r was US\$ 453 per person per year in low-income countries, and US\$ 442 in upper-middle-income countries (Fayorsey et al., 2013). Several factors have contributed to the price trend for second-line regimens since the mid-2000s. They include decreases in the prices of Abacavir, LPV/r and TDF and the prequalification of generic versions of LPV/r (Eholie et al., 2012). Greater economies of scale, new pricing policies by research-based pharmaceutical companies and efforts to expand the market for second-line regimens also contributed (Estill et al., 2016). Although these developments are encouraging, addressing the relatively higher cost of second-line regimens is an important priority for both resource-poor countries and developed countries.

clinicians perceptions to antiretroviral drugs.

Often, clinicians working in HIV care and treatment clinics do not trust WHO criteria for diagnosing and detecting ART treatment needs due to the poor reliability of clinical and immunological assessments (Ramadhan et al., 2014). Clinicians' skepticisms of WHO criteria may contribute to the low number of patients switched to second-line ART globally (Bacha et al., 2012; Eholie et al., 2012; Kumarasamy et al., 2012). Another trouble may be on drug interactions, as the concomitant use of ART and traditional medicine can result in drug interactions. This problem with drug interactions was noted during an Indian study, which indicated perceptions of drug side effects and interactions made clinicians reticent to switch patients to second-line ART, despite poor prognosis with routine viral load monitoring (Kumarasamy et al., 2012).

Drug interactions for patients on ART can be significant. For example, during a study on ARV interactions, Jourdain et al. (2013) found that saquinavir, when combined with other medications such as ritonavir, can cause irregular heartbeats (Jourdain et al., 2014). Thus, in addition to the expense and poor access, drug interactions may cause reticence among clinicians when it comes to switching patients to second-line ART (Ramadhan et al., 2014; van Zyl, 2012). The lack of adequate ART regimens and problems related to treatment adherence and interactions restrict clinicians from transferring patients to second-line ART. Even when patients are aware of ART goals, clinicians may hesitate to place patients on appropriate ART for a number of reasons such as; (a) ART toxicity, (b) issues related to quality of life, and (c) fears of long-term adverse drug reactions (Ramadhan et al., 2014).

Switching therapy for issues related to quality of life or fear of possible toxicity is only acceptable if these factors compromise ART adherence. Often, patient compliance may suffer if negative side effects are experienced (Murphy et al., 2012). It is important for clinicians to fully discuss issues of drug toxicity with patients to encourage treatment adherence (NYS- DHAI, 2015). It is therefore recommended that clinicians prescribe ART that is best at delaying viral replication, delaying illness development, and improving quality of life for patients (WHO, 2013b). There should be a mutual relationship between clinicians and patients to decide when to start ART. Both advantages and disadvantages of using ART be discussed and agreed upon between clinicians and patients.

burnout and stress

Burnout refers to the inability to cope with natural surroundings due to work demands (Skills You Need, 2014). It is a situation in which one loses interest in working, due to long-term fatigue, and may occur when someone is overworked for an extended time, or experiences constant tension (Guarinoni et al., 2013). A number of people are at-risk of burnout due to external tensions, and others may suffer burnout without any significant pressures (Gilbert, 2014). People suffer from burnout when there is an imbalance between demands placed on them and the mechanisms available to them to cope with those demands. Common reasons for burnout include a lack of control over their work, lack of organizational support from team members, lack of resources, training or support needed to do your job and poor work/life balance (DeMers, 2015).

Unfavorable working conditions in the absence of motivations, incentives and poor recognitions to clinicians working at HIV clinics decreases morale of clinicians to concentrate with patient's health as most of them are subjected to burnouts. This calls for discussions to mitigate it. Research indicates high rates of burnout among individuals in public positions, such as public health workers (Shanafelt et al., 2012). Approximately 46% of clinicians' experience at least one symptom of burnout (Shanafelt et al., 2012). Moreover, burnout is more prevalent among clinicians than any other educated profession (Shanafelt et al., 2012). Work-related burnout affects employees, as well as employers; it actually impacts the performance of the workplace as a whole (Guarinoni et al., 2013).

Individual performance is compromised because burned out workers need to invest extra time and effort in performing their job (DeMers, 2015). Additionally, collective performance may suffer because healthy employees spend time in helping their sick colleagues, at risk of also damaging their own health and their professional (Dachis, 2012). Burnout increases absenteeism, reduces productivity, and creates high rates of employee turnover (Guarinoni et al., 2013). Therefore, it is in the interest of companies to address employee burnout to boost personnel psychological health and improve productivity.

Evidence shows that many factors can instigate burnout. Some of these factors include: shift work, night work, rigid work environments, inconsistent work schedules, extensive work hours, meaningless work, inconsistency working rotations, underuse of skills, inadequate equipment, isolation, poor employer/employee relationships, lack of

decision making, lack of professional advancement, indecision, and poor salaries (Guarinoni et al., 2013).

Burnout negatively affects the performance of many clinicians, and is linked with poor health conditions, such as stress-related illness (Guarinoni et al., 2013). Burnout also impairs cognitive capabilities (Shanafelt et al., 2012). In terms of its effect on patients, clinician burnout is related to low levels of patient satisfaction, prolonged post-surgical recovery, and increased rates of clinician mistakes (Shanafelt et al., 2012). Limited resources and time may also cause HIV clinicians to experience burnout. Clinicians often work in health centers that serve HIV patients, so adequate resources, time, and strong relationships with coworkers may affect their decision-making abilities, such as knowing when to transfer patients to second-line treatment (AHRQ, 2012). Clinicians often face obstacles that place their personal and professional survival at risk (Imtiaz & Ahmad, 2015).

Researchers compared job satisfaction with turnover intentions due to work stress and found clinicians were more likely to experience low job satisfaction if they felt stressors made them unable to remain competent in their field (Imtiaz & Ahmad, 2015). Clinicians are subjected to stresses conditions that puts them into poor working performance which then, makes them inactive and therefore, causing poor management of PLHIV as they attend them during their scheduled visits at HIV care and treatment health facilities. Major steps are required to prevent burnout among clinicians. A negative link exists between work-stress and job performance (Manzoor, Awan, & Mariam, 2012). Employees with high stress levels often demonstrate low job

performance. These factors affect a greater number of male than female employees and increases clinicians' chances of making serious mistakes when it comes to patient assessment switching patients to second-line ART (Imtiaz & Ahmad, 2015). Job satisfaction is required among clinicians in order to make them effective on rendering HIV services to PLHIV.

adherence and retention to antiretroviral drugs.

Adherence to ART means sticking firmly to treatment regimen by taking HIV medicines every day and exactly as agreed between clinician, client and treatment supporter, in case of minors (Hansana et al., 2013). Adherence has been correlated strongly with HIV viral suppression, reduced rates of resistance, enhancing survival, improving life expectancy and preventing the spread of HIV to partners and offspring (CDC, 2016). Adherence to ARV's medication is a critical aspect for HIV treatment success (WHO, 2016). And it is required at a rate of >95% to maximize the benefits of ART (Murphy et al., 2012). Because it is difficult to maintain such rates, Odendal (2014), has advised that HIV programs across the world should use continuous and supportive adherence counselling for people on ART medication.

Efforts should be made toward suppression of an individual's HIV in the body than curing AIDS (Hansana et al., 2013). As such, attaining the required level of ARV drug adherence is important because viral suppression cannot be achieved when ARV drugs are not used as prescribed, and for life (Ciaffi et al., 2015). And that, poor ARV medication causes transmutations of the virus and later drugs resistant (Carter, 2012). Findings from Uganda study revealed that improper adherence to ART leads to poor

suppression of HIV replication of individual infected cells and therefore increasing prevalence of HIV in the community (Buyu et al., 2016).

Lack of ART adherence, promotes transmission of drug resistant HIV among individuals in the community (Schaecher, 2013). Drug resistance causes first- line treatment failure (Levison et al., 2012). Adherence should be considered as an important aspect for successful HIV treatment. Previous studies denote that the risk of emergence of drug resistance with suboptimal adherence is generally greater in patients taking NNRTIs compared with most PIs (Carter, 2012), and that adherence was improved in subjects randomized to switch from a PI to EFV or to ABC compared with those who continued the PI based regimen (Van Zyl et al., 2012). Other investigators have reported improvements in quality of life, as assessed by questionnaires, in two randomized studies in which PIs were switched to NVP or to either NVP or EFV compared with continuing the PI (CDC, 2014).

the role of clinicians in ART adherence

Before writing the first prescription(s) for patients initiating or reinitiating ART, clinicians should assess the patient's adherence readiness. Clinicians should evaluate patients' knowledge about HIV disease, treatment, and prevention (Meintjes et al., 2014). In addition, clinicians should assess patients' motivation to successfully adhere to ART and identify and support facilitating factors and address potential barriers to adherence (NACP, 2015a). Finally, clinicians should be assured that patients have the necessary medication taking skills to follow the regimen as prescribed (Joglekar et al., 2012). On the other hand, clinicians are required to have skills that will make them able to provide

successful ART adherence and making sure that patients are maintained and retained into ART (Green et al., 2014).

In South Africa where implementation of a clinical mentorship for ART program is practiced to clinicians, patients ART adherence is higher because clinicians initiates ART to majority of eligible patients, they manage HIV and AIDS complex cases (Republic of South Africa-Health Department [RSAHD], 2014). Mentorship can increase clinical confidence and enhance professional development (Green et al., 2014). Clinical mentorship should be considered essential for universal ART access in resource limited settings as well influencing willingness to adhere on ART among HIV patients (Meintjes et al., 2012).

ART is rarely initiated during first round attendance but rather two to three visits are usually required to provide patients with adherence counseling (Wilkinson, 2014). In this case, patients must demonstrate their abilities to visit care and treatment clinics regularly to obtain medication and that, clinicians are required to provide patients with adherence counseling prior to initiating ART in order to prevent drug resistance (Bateman, 2013). Second-line ART may be deferred when there is indication of poor adherence to first-line ART.

Summary and Conclusion

Many studies have been conducted to explore factors and facilitators of ART adherence (Barnett et al., 2013; Wasti et al., 2012), including retention (Christopoulos et al., 2015; Freya et al., 2014), VL monitoring as a predictor of switching patients to second-line ART (Chkhartishvili et al., 2014), and facilitators of ART to patients at HIV

clinics (Tsoi, 2013). This review of available literature indicated a dearth of research on the barriers that influence clinicians' decisions to transfer patients to second-line therapy. Thus, this qualitative research has explored clinicians' knowledge, experiences and perceptions related to low percentages of switching patients into second-line ART, a challenge that is facing Tanzania (Ramadhan et al., 2014).

Little information currently exists on predictors of first-line and second-line treatment failure among patients in HIV programs (NACP, 2012). Many of these programs utilize WHO criteria to monitor patient success (NACP, 2013b). A recent study conducted in Tanzania indicated a resistance level of 14.8% to first-line ART patients (Kasang et al., 2012). Thus, one must ask why clinicians are not switching these patients to second-line therapy. The barriers that prevent clinicians from switching patients to second-line ART have not been explored. This study has used the PAR theoretical framework to explore barriers that may influence clinicians' decisions to switch patients to second-line ART.

Six key thematic areas were identified for analysis and for results interpretation. These include; (a) capacity of clinicians to diagnose treatment failure, (b) laboratory investigations, (c) cost and tolerability to second-line ARV drugs, (d) clinicians' perceptions on second-line drugs, (e) adherence and retention to ARV drugs, and (f) burnout/stress. The following Chapter 3 provides details on the study methodology for this study.

Chapter 3: Research Method

Introduction

The possible factors that may influence clinicians' decisions to transfer patients to second-line ART was detailed in chapter two. This research had explored the reasons as to why clinicians in Tanzania decides against transferring patients to second-line ART. This chapter details the study methodology, including participant selection criteria, data collection, and data analysis procedures.

Research Design and Rationale

This is a qualitative study design that aimed at providing detailed, rich data surrounding the research questions of the topic in research (Tracy, 2013). Qualitative methods are helpful for exploring people's interpretations of experiences (Creswell, 2014). Quantitative methods are employed to statistically test and analyze predetermined variables. Because the goal of this study was to conduct an in-depth exploration of barriers that may influence clinicians' decisions to switch HIV patients to second-line ART, a qualitative methodology was chosen. I considered several designs for this study, including phenomenology, ethnography, grounded theory, and case study. However, I selected a descriptive design (Aschengrau & Seage, 2014) due to its ability to explore systematic knowledge in new areas of inquiry (Berg & Lune, 2012).

A primary component of descriptive information is the concise and quantifiable description of the situation in question. The best descriptive information must answer the five essential *W questions* (i.e., who? why? where? what? when), and possibly, the extra sixth W - so what? (Berg, & Lune, 2012). A descriptive qualitative study is used to

investigate human behavior by gathering, analyzing, and understanding the words and events of people or communities (Yin, 2014). As a researcher, I used a qualitative study design to generate understanding of issues from the perspective and in the language of the clinicians. A natural setting of clinicians was used to inquire ARVs treatment information and for that matter, I'm happy to say that clinicians were very enthusiastic to provide data openly with real examples from patients they see in HIV care and treatment health facilities

Research Questions

To inquiry issues related to the topic in the research, the following research questions were addressed:

RQ1: What factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

RQ2: What are clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

RQ3: What factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

Researchers Roles

Investigator serves as the research instrument in qualitative studies (Tracy, 2013). For this study, I personally collected data and conducted data and analysis. When conducting interviews for data collection, I was aware of my personal bias and limited them by performing epoché and bracketing (Moustakas, 1994). Though performing

epoché and bracketing I was to suspend my personal beliefs and opinions in order to obtain an unbiased understanding of barriers that may impede clinicians from switching patients to second-line ART.

Methodology

participant selection

Study participants included clinicians, such as nurses (nursing officers and nurse midwives), pharmacists (pharmaceutical technicians and pharmacists), and doctors (medical doctors, assistant medical officers, clinical officers, and assistant clinical officers). All participants were located in the three Municipals of Dar es Salaam city, including Kinondoni, Ilala, and Temeke. I purposively used sampling technique to recruit 30 clinicians working in HIV care and treatment clinics from the three municipalities. I selected six clinicians from referral hospitals of the three municipalities (two each from Temeke, Amana and Mwananyamala hospitals). Twelve clinicians were selected from the six health centers (one health center from rural and other one from urban for the three municipalities), and finally I recruited 12 clinicians from the six dispensaries within the three municipalities (one dispensary from rural and other one from urban for each municipal).

sampling framework

I applied purposive sampling technique, which is a kind of a nonprobability sampling used to obtain participants with specific characteristics (Creswell, 2013, 2014; Maxwell, 2013). To qualify for the study, all participants (clinicians) had with the following inclusion criteria: (a) being trained to provide HIV care and treatment services, (b) having at least 12 months working experience at care and treatment clinics, (c) being

fluent in speaking and comprehending Swahili and/or English, and (d) clinicians having greater knowledge on HIV routine data management. Sample size requirements for qualitative studies depend on saturation, or the point at which the addition of new participants does not result in new themes (Tracy, 2013).

Several researchers have provided recommendations for the size of initial samples in qualitative studies. For example, Francis et al. (2012) recommended 10 to 13 participants, while Morse (1994) recommended a sample size of at least six participants. Tracy (2013) recommended for five to eight participants. In this study, I selected a sample of 30 participants. Although this was larger than most recommendations, I opted to have a larger sample in order to ensure saturation and information depth.

instrumentation

Data were collected through my own developed interview protocol/guide which had with semi structured, open-ended questions to allow me explore the interviews in depth. The instrument was developed based on clinicians working environments and literature review in which no challenges that arose during the development process because all participants were involved in the review of the protocol before the interviews commences. I followed up each interview question with probing questions to draw out details on participants' experiences and perceptions. I also scheduled another round of interview to some participants in case of no sufficiency data for analysis. According to Yin (2014), open-ended interview questions can improve data analysis and credibility, while reducing researcher bias.

According to Otieno, Obondo, and Mathai (2012), researchers can apply in-depth interviews, focus group discussions, brainstorming, role plays, market place discussions, spider diagrams and Venn diagrams, ranking and scoring, and displays star charts methods to facilitate and encouraging participation during the PRA process. These methods help the participants to identify priority areas for actions. In this study, I used an in-depth interview to explore reasons as to why clinician's delays switching first-line to second-line ART. I also used fieldnote, observations and audio recording to collect sufficient data from participants. To maintain data integrity, I engaged in bracketing and epoché, which involves the awareness and suspension of preconceived ideas (Yin, 2014).

Prior to data collection, the interview protocol was reviewed by a panel of subject matter experts, including the Regional and Districts AIDS Control Coordinators, in-charges from Care and Treatment Clinics. Members of the panel reviewed the protocol questions to ensure that they are appropriate to the study, free of bias, and are not leading. I used all potential recommendations provided by the panel expert to revise the interview protocol. The panel review was used to validate the protocol in lieu of a pilot test.

recruitment procedures, participation, and data collection

After having permission to conduct this study from the Walden University's Institutional Review Board with an approval number (08-29-16-0309530), I contacted all HIV care and treatment centres located in the three Municipals of Dar es Salaam city, Tanzania, including Kinondoni, Ilala, and Temeke to inform organizational leaders about the study. After obtaining permission to use each location as a study site, I posted informative flyers at the study sites to invite clinicians onto the study. I wrote formal

letters and posted it to the study sites. I provided my contact information on the flyers and letters so interested participants can inquire about the study. After I had spoken to all prospects to ensure that they meet participant inclusion criteria, I scheduled individual, in-person interviews with each participant at a location and time that is convenient to them. Interview locations were quiet and free from distractions.

Before interviews commence, I reviewed the informed consent form with participants and answered any study-related questions asked. Participants were informed that their involvement to this study was completely uncoercive and that, whoever wishing to terminate participation was allowed to do so without a penalty. I informed all participants that interviews were to be audio recorded, and participants had the opportunity to review data analysis to make sure that what I captured from interview were accurately captured their thoughts. Any individual who refused to sign the consent form was thanked for his or her time and was removed from the study. Individuals who signed the consent form were provided with an additional copy of the form for their records.

After I had a signed consent form from individual participant, I started data collection through an in-depth, open-ended interview, following the validated interview protocol. Data were collected from 5th September to 7th October 2016. I interviewed participants with open-ended questions to allow me control the flow of the dialogue in relation to the research topic (Creswell, 2013, 2014; Trainor, & Graue, 2013; Yin, 2014). I used approximately 30 to 45 minutes for each interview. Adding to audio taping in the interviews, I put summary of important observations into a sheet in order to record nonverbal communications plus other additional observations. The sheets were used as

field notes and were translated into descriptions for data analysis (Emerson, Fietz, & Shaw, 2012).

During this time memos were as well developed and kept as a benchmark for data analysis. All study-related data are kept in a safety place to prevent anyone else from accessing it. I thanked individual participant for their time and contributions immediately when I had finished the interview. I also made appointments with participants for second or third rounds of interviews where need be. After the transcriptions and data analysis are complete, each participant was provided with a copy of his or her interview transcript to review its accuracy and provide potential comments to make it sound. This allowed for member checking where I confirmed data accuracy and its legitimacy (Yin, 2014).

data analysis plan

I transcribed data from the interview transcripts verbatim (Saldaña, 2014), and I then uploaded transcripts into Atlas.ti.7.1.3 (Yin, 2014) to assist with data organization. Atlas.ti.7.1.3 was used to assist with the facilitation of data coding. I performed a coding procedure to allow me to enter the data into the Atlas.ti.7.1.3 software analytical package. I created a deductive coding and labelling for sub-categories and major categories for thematic information and inductive coding for emergent themes; a priori codes were identified from research question and the literature review, while emergent codes were generated from interviewees' responses transcripts (Schreier, 2012). The use of both a priori and emergent codes is encouraged by Creswell (2013, 2014) as a technique to improve thematic analysis from interviewees' responses.

I employed Yin's (2014) framework to identify factors that influence clinicians' decision-making processes regarding second-line ART. Yin also explained that model matching and narrative techniques are the best methods for data analysis. Model matching involves looking for contrasting models within existing findings with previously acknowledged models from the literature. The aim of narrative techniques was to clarify *how* or *why* an event occurs (Yin, 2014). These techniques were applied in this study to compare respondents' models of experiences or/and practices to address the stated problem of the study.

issues of trustworthiness

In qualitative research, rigor is established through credibility, transferability, dependability, and confirmability (Seale, 2012; Yin, 2014). Credibility is the degree to which participants' perceptions and experiences are accurately reflected in the data (Lincoln & Guba, 1985). Credibility can be reinforced in multiple ways. For example, Creswell (2014) made the following recommendations for improving research credibility: (a) prolonging engagement with participants, (b) choosing appropriate participant selection criteria, and (c) employing appropriate sampling methods. In addition, credibility can be improved through researchers' mindfulness of how their behaviors could influence participants. To remain mindful and prevent personal bias from tainting study results, I engaged in bracketing and epoche but also a member checking exercise to improve study credibility (Moustakas, 1994).

Member checking involves allowing participants to review preliminary analysis of interview transcripts to ensure the researcher has accurately interpreted their

experiences. Transferability describes the generalizability of study findings (Merriam, 2013). Transferability is not an aim of qualitative study; however, it can be improved with thick description and rich contextualization. Although findings from this study will not be transferable to other settings and populations, they will provide information that may apply to other situations related to the ART switching processes (Yin, 2014). A study's dependability refers to its ability to be replicated (Yin, 2014).

To ensure dependability, I documented all steps of the data collection and analysis process with detail. This process is, known as an audit trail, which include documentation of any methodological deviations that occurred from the plan as detailed in this chapter. In addition, I engaged a reflexive clarification to improve study dependability (Seale, 2012). Finally, I ensured confirmability of my study through the inclusion of credibility, transferability, and dependability procedures (Yin, 2014).

ethical procedures

Prior to any data collection, I requested a study endorsement from Walden University's IRB. Following the Walden IRB authorization (with an approval number 08-29-16-0309530), I also sent details of my study to the National Institute for Medical Research (NIMR) because all studies involving human subjects in Tanzania requires ethical clearance from the NIMR. To ensure that all participants are treated in a fair and ethical manner, I followed the Basic Ethical Principles outlined in the Belmont Report (DHHS, 1979). It is from the Belmont Report where we see that all research participants requires to be provided with justice and beneficence. During data collection, my primary concerns were to ensure that the well-being of each participant is held to the highest

standard. To do this, my research was highly designed to a way that it minimizes risks to any participant.

By following principles outlined by the Belmont Report and Walden University's IRB, the study's utility was maximized while minimizing threats to participants.

Participants' identities are being protected through the assignment of a numerical value, based on order of interview, in lieu of any identifying information. Additionally, identifying information will not be included in presentations or publications of the research. Individuals who participated in the study had an option to leave the study immediately when they wished to do so and in the absence of any expenses. Participants were given autonomy to sign an informed consent, which included details of the study and my contact information.

Prior to interviews, I reviewed the informed consent form with each participant to go over study risks, benefits, objectives, and confidentiality procedures. All participants had the opportunity to ask questions prior to data collection. Any participant who refused to sign the informed consent form was thanked for his or her time and removed from the study. All physical documents related to this research are kept in a safety place to which only I access it. These physical documents include paper files, audiotapes, and hard copies of interview transcripts. All electronic files are also kept in a separate, password-protected external hard drive, to which only I, have the access.

Summary

This chapter has described the research methodology of the study. The next chapter depicts the research findings

Chapter 4: Research Findings

Introduction

The intention of the research was to establish and describe the barriers that influence clinicians at making decision in transferring HIV adult patients into second-line ART. Findings of this study will provide clinicians with strategies that will easily help them to discover first-line treatment failure to their patients and switch these patients into second-line ART at the earliest appropriate time.

Research questions included the following:

RQ1: What factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

RQ2: What are clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

RQ3: What factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

This chapter starts with a description of the study setting and participant demographics. The next section of the chapter includes the procedures that was used to collect and analyzing data. This chapter further includes evidence of trustworthiness that comprise of credibility, transferability, dependability, and confirmability of the findings. Finally, the next section includes results while basing on the PAR theoretical framework.

Setting of the Study

This study was conducted from the three Municipals of Dar es Salaam city, including Kinondoni, Ilala, and Temeke. I employed a purposive sampling technique to recruit clinicians working in HIV CTC from the three municipals. Six clinicians were selected from referral hospitals of the three municipals (two each from Temeke, Amana and Mwananyamala hospitals). Twelve clinicians were again selected from the six health centers (one health center from rural and other one from urban for the three municipals), and finally I selected 12 clinicians from the six dispensaries within the three municipals (one dispensary from rural and other one from urban for each municipal). The selected participants were those who met the criteria including training on HIV management and with at least 12 months working experience in CTC and who volunteered themselves to participate in the interview. I was able to randomly receive 30 participants and had 100% response rate.

I applied a purposive sampling approach to recruit participants as well as posting informative flyers at the study sites, writing emails and phone calls to invite participants for the study (Appendix B, Appendix C, and Appendix D). Prior to data collection, I wrote letters to request permission to conduct this study into Kinondoni, Ilala and Temeke municipals (Appendix E). I conducted a member checking with HIV care and treatment experts for the protocol questions to ensure that questions were appropriate for the study, free of bias, and were not leading. I used the recommendations provided by the panel to revise my interview protocol. The panel review was used to validate the protocol in lieu of a pilot test.

After I had spoken with prospects who met inclusion criteria to participate in the study. I then scheduled individual, in-person interviews with each participant at a location and time that was convenient to them. Interview locations were quiet and free from distractions in such a way that no participants miss the interview. Before interviews commence, interested participants were given a written informed consent form to sign. Individuals who signed the consent form were provided with an additional copy of the form for their records. I explained the study purpose and requirements to participants in order for them to have a full information about it. I collected data through an in-depth participant interviews while using a semi-structured interview guide/protocol coupled with extensive probing per each interview question.

I modified the data collection tool to meet the recommendations that was made during the member checking by the panel experts. They recommended that all questions should be arranged in chronological order as per the research questions (Appendix A). At the end of interview each participant was given 10,000 Tanzanian shillings as a disturbance allowance. In addition to the interviews, I also conducted audio recording, field observations, and took field notes to record nonverbal communications. Field notes were taken during interviews and were translated into descriptions for data analysis. Participants identifications such as faces, images, emails, phones and addresses were detached from the transcription and a numerical pseudonym with an alphabetical letter “P1 to P30” was given to all participants.

All study-related data were kept in a safe place to prevent anyone else from accessing it. After transcription is complete, each participant was provided with a copy

of his or her interview transcript to allow for member checking and confirm data accuracy and legitimacy (Yin, 2014). Immediately after I had collected that, I prepared memos, translated interviews from Swahili to analytical language (English language). I then transcribed interviews, coding them deductively, labelling, and imported transcripts into Atlas.ti.7.1.3 analytical software package that facilitated analysis. I analyzed data after I had categorized it in six thematic areas namely; (a) capacity of clinicians to diagnose first-line treatment failure, (b) laboratory investigations, (c) availability, accessibility and tolerability to second-line ART; (d) clinicians' perceptions on second-line drugs; (e) Readiness to second-line medicines and, (f) adherence and retention to second-line medicines.

I critically observed ethical clearance by obtaining IRB approval to conduct my study . To maintain data integrity, I engaged a bracketing and epoché method to suspend my preconceived ideas relating to the topic in research (Yin, 2014). I conducted an audit trail, cyclical and iterative data collections with participants in order to maintain trustworthiness of my study. Findings from this study will impact positive social change to public health professionals on the knowledge that is valuable to improve HIV management across the country and globally.

Demographics

A total of 30 clinicians including nurses (nursing officers and nurse midwives), pharmacists (pharmaceutical technicians and pharmacists), and doctors (physicians, medical doctors, assistant medical officers, clinical officers, and assistant clinical officers) participated in the study. The roles of physicians are to assess patients'

eligibility for ART initiations, patients' history taking and physical examinations, and prescribing ART for HIV patients at each visit. The roles of pharmacists are to dispense ARV medicine and conducting pill counting exercise for patients on ART in each visit and the role of nurses is to provide pre/post counselling and testing for HIV to individuals, and ART support and adherence counselling for PLHIV in order to retain them into care and treatment services. Table 1 below presents characteristics of participants and table 2 displays detailed description of participants in the study.

Table 1.

Participants Characteristics

| Characteristics of participants | Number of participants |
|---------------------------------|------------------------|
| Male | 15 |
| Female | 15 |
| Carders | |
| Physicians | 0 |
| Medical Doctors | 6 |
| Assistant Medical Doctors | 7 |
| Pharmacist | 4 |
| Clinical Officers | 9 |
| Assistant Clinical Officers | 0 |
| Nurses | 4 |
| Working experience at CTC | |

table continues

| | |
|---------------------------------|------|
| Characteristics of participants | 70 |
| Number of participants | |
| 1 year | 4 |
| 2 years | 6 |
| 3 - 5 years | 9 |
| Above 5 years | 11 |
| Average Age | 30.5 |

Table 2.

Participants Particulars

| Participant ID | Roles | Sex |
|----------------|---|-----|
| P1 | Nurse ART Provider | F |
| P2 | Medical Doctor ART prescriber | M |
| P3 | Assistant Medical Officer CTC manager | F |
| P4 | Medical Doctor ART prescriber | M |
| P5 | Assistant Medical Officer ART prescriber | F |
| P6 | Nurse ART provider | F |

table continues

| Participants ID | Role | Sex |
|-----------------|---|-----|
| P7 | Medical Doctor ART prescriber | F |
| P8 | ART Pharmacist | F |
| P9 | Clinical Officer ART prescriber | M |
| P10 | Nurse ART Provider | F |
| P11 | Medical Doctor ART prescriber | M |
| P12 | ART Pharmacist | F |
| P13 | Assistant Medical Officer ART prescriber | M |
| P14 | Medical Doctor ART prescriber | F |
| P15 | Assistant Medical Officer ART prescriber | F |
| P16 | ART Pharmacist | F |
| P17 | Clinical Officer ART prescriber | F |
| P18 | ART pharmacist | F |
| P19 | Assistant Medical Officer ART prescriber | M |

table continues

| Participants ID | Roles | Sex |
|-----------------|---|-----|
| P20 | Nurse ART provider | M |
| P21 | Assistant Medical Officer CTC manager | F |
| P22 | Clinical Officer TB/HIV Officer | M |
| P23 | Medical Doctor ART prescriber | M |
| P24 | Clinical Officer ART prescriber | M |
| P25 | Clinical Officer ART prescriber | M |
| P26 | Assistant Medical Officer ART prescriber | M |
| P27 | Clinical Officer ART prescriber | M |
| P28 | Clinical Officer ART prescriber | M |
| P29 | Clinical Officer ART prescriber | M |
| P30 | Clinical Officer ART prescriber | F |

Presentation of Findings

Data Collection

In this study, data were collected from 30 participants using semistructured, open-ended questions, which allowed me to explore the research interviews in depth. Data were collected from clinicians working at CTC in Dar es salaam city. I conducted interviews while probing questions to draw out details on participants' experiences and perceptions. These methods helped participants to identify priority areas for actions. Data were collected from 5th September through 7th October 2016. An iterative and cyclical data procedure was applied in occasions where there were no sufficient data extracted from participants for data analysis. Immediately after data collection I developed field memos that helped me the data analysis process. At the end of an individual interview, I prepared a transcript before I leave from the field and in order to easily memorize the interviews concept. During data collection, there was variation on data related to a question burnout/stress. None of the participants had responded on this question and therefore, it was not considered for analysis.

According to Yin (2014), bracketing and epoché methods helps researcher to validate data, I applied this method to maintain data integrity. As such, prior to data collection, I had to review the interview protocol with participants as well the panel of subject matter experts, including the Regional and Districts AIDS Control Coordinators, in-charges from Care and Treatment Clinics. Members of the panels reviewed the protocol questions to ensure that they were appropriate to the study, free of bias, and are

not leading. I used all recommendations provided by the panel to revise the protocol.

The panel review was used to validate the protocol in lieu of a pilot test.

Participants to participate in the study were in-person scheduled for interview at a location and time that is convenient to them. Interview locations were set in a quiet and free from distractions and that, all participants were given a written informed consent form to sign before they participate in the study. Individuals who signed the consent form were provided with an additional copy of the form for their records. At least each interview took an average of 30 to 45 minutes. The interview was complemented by audio recording of the interviews and field notes to record nonverbal communications and additional observations. Field notes were taken during interviews in order to facilitate translation of data for data analysis (Emerson, Fietz, & Shaw, 2012).

Data Analysis Strategy

Upon completion of the interviews, I first translated data from Swahili to English for analysis. The translation activity was followed by transcription of in person interviews into electronic format to combine all participant responses from the interview data. Then, a first cycle deductive coding with concepts was conducted as per research questions before being exported to the Atlas.ti.7.3.1 analytical software. Individual electronic transcripts were then exported into the Atlas.ti.7.3.1 and the initial coding phase was completed through the process of structural coding. Process of structural coding is designed to start organizing data around specific research questions and thematic area (Yin, 2014). In this context, a total of 336 segments were coded in 11 identified categories from the 30 participants electronic word transcripts.

Table 3.

Categories and Codes from Participants Transcripts

| Categories | Coded segments |
|---|----------------|
| Knowledge | 45 |
| Competence | 11 |
| Experience | 7 |
| Viral-load and CD4 Testing | 66 |
| WHO eligibility criteria for HIV & AIDS treatment | 71 |
| ARV medicines side effects | 35 |
| Costs for ART | 33 |
| Drugs resistance | 28 |
| ART readiness | 32 |
| Supportive counseling for ART | 62 |

Throughout the coding method, commonalities were developed. I journalized memos of patterns and themes occurring in the data for later reference. Once codes were categorized, they were compared to one another. Next, a second cycle pattern coding method (Saldana, 2013, p. 49) was used next to recognize similarly coded data and further summarize it categories or consolidate as shown in table 3. I also used a thesaurus (Microsoft, 2013) to help me better refine coded words, then, I applied a third level of coding, the axial coding method (Saldana, 2013, p.152) to further analyze results

from the first two stages and discovered the following major six themes for analysis (a) clinicians capacity to diagnose treatment failure, (b) laboratory investigations, (c) availability, accessibility and tolerability of second-line drugs, (d) clinicians perceptions to second-line drugs, (e) Patients readiness to second-line drugs and, (f) Adherence and retention to second-line drugs. Each theme was then interrelated with categories for analysis (Saldana, 2013, p.152). Because triangulation helps researchers to analyze data, I applied this method to analyze findings of this study (Saldana, 2013, p.153).

Evidence of Trustworthiness

I critically observed the ethical clearance issues through obtaining IRB approval notification email that allowed me to conduct the study. An approval number for this study is 08-29-16-0309530, with the expiration date of August 28, 2017. According to Yin (2014), bracketing and epoché method helps researchers to maintain data integrity of their study, I used this method to suspend my preconceived ideas in relation to the topic in research (Yin, 2014). I provided a signed copy of a written informed consent to all participants in the study. I conducted audit trail, cyclical, and iterative data collections with participants. To maintain dependability of data I ensured that all the steps used during data collection and analysis process were documented in detail. I understand that, findings from this study may not be transferable to other settings and populations; however, recommendations provided in this study will be applicable in other situations related to ART switching processes. Indeed, the study methodology can be used elsewhere for studies relating to HIV management.

Results by Thematic Areas and Research Questions

About 28 participants admitted to have low knowledge, competence, and experience on second-line ART. Having low capacity in diagnosing first line treatment failure makes them either fail to provide the medications correctly to patients or provide correct information to patients who are in need of second line ART. For example P9 had stated that he would like to be reminded on new ways of proper history taking and physical examination for patients as this will equip him with knowledge and concepts of patients management and care. P4 recommended the following:

“There is a need for clinicians to have additional trainings on proper history taking and examination for their patients to establish first line treatment failure and switching them to second line. Now days, clinicians are not competent on this aspect”

P12 had the view that provision of second-line ART to PLHIV would be appropriate if all clinicians in CTC are fully provided with the skills on how to manage HIV patients because having inadequate knowledge on this aspect will continue to delays transferring of their patients to second-line ART. Some of the clinicians are not aware on various categories of second-line ART leave alone even those in first-line. For example, P2 had stated that it is difficult for most of clinicians to provide second-line ART to patients because, majority of them are not yet been trained for that services despite the government efforts that insists clinicians to do so. Topping to what has been stated by P2, participant 11 had lamented by saying;

“Look here my friend, you are not trained to give second line ART to patients but yet, the government insists you to do so, tell me, how do you start?”

P5 had explained that lack of exposure to the newly recruited clinicians poses a great challenges in managing patients at CTC both with the first-line and second-line ART. New employees are not trained on ART provision when they are at medical training schools and so, they often lack knowledge and skills for HIV management and. when employed some of these employees are either oriented or trained by the government or sometimes with HIV implementing partners to provide HIV services to PLHIV. Others receives the knowledge through periodic national, regional and district supportive supervisions. In the case that there are no such initiatives these clinicians are left to practice in CTC without experience and in order to fill the existing critical shortage of human resource for health in Tanzania.

Participants recognize the efforts that the Ministry of Health is doing in updating the medical training curriculums with HIV management topics that aims at equipping medical professionals with a vast knowledge on HIV care, treatment and supports in order to increase skills and practices while in the field. Despite this efforts, , participants had claimed that they do not have exposure to clinical management of HIV & AIDS and so, this limit them to adequately assess patients readiness for ART. Participants explained that, they normally depend on history taking and physical examinations to initiate ARV to PLHIV. They said that, it may have been nice for them if they would have been provided with modern technologies such as VL testing to assist them identify the treatment failure for patients they serve. To further support on this statement one participant had specifically said

“Let us be frank Mr., we do not have exposure to clinical management of HIV & AIDS, this limit us to adequately assess patients’ readiness for ART. We normally depend on history taking and physical examinations to initiate ARV to PLHIV. May be if we could have modern technologies such as viral load testing it could have assisted us to identify the treatment failure” (P6)

Table 4.

Thematic Area and Categories for RQ1

| Major themes | Categories | Quotes from participants |
|--|------------|---|
| Capacity of clinicians to diagnose treatment failure | Knowledge | Look here my friend, you are not trained to give second line ART to patients but yet, the government insists you to do so, tell me, how do you start? (P11). |
| | Competence | There is a need for clinicians to have additional trainings on proper history taking and examination for their patients to establish first line treatment failure and switching them to second line. Now days, clinicians are not competent and do not have experience on this aspect (P4). |

table continues

| Major themes | Categories | Quotes from participants |
|--------------|-------------|---|
| | Experiences | Let us be frank Mr., we do not have exposure to clinical management of HIV & AIDS, this limit us to adequately assess patients' readiness for ART. We normally depend on history taking and physical examinations to initiate ARV to PLHIV. May be if we could have modern technologies such as viral load testing it could have assisted us to identify the treatment failure (P6) |

estimated time for second-line switching

Findings shows that all 30 participants who participated in this study had inconsistency ART modification or transferring timing. Having no knowledge or idea on when to shift patients into second-line ART is another reason that makes them delays in making decision for transferring patients into appropriate regimens. Table 5 below shows the time elapsed from first line ART treatment failure to patients shifting into second-line ART.

Table 5.

Time Elapsed for Switching Second- line ART

| I don't know | 1wk | 2wks | 1month (4 wks) | 3moths (12wks) | 6months (24wks) | 1year (52wks) | 1.5years (76wks) | 2years (104wks) | Total |
|-----------------|-----|------|-------------------|-------------------|--------------------|------------------|---------------------|--------------------|-------|
| 10 | 4 | 5 | 3 | 2 | 2 | 2 | 1 | 1 | 30 |

laboratory investigations

Majority of participants had seen the importance of using laboratory technologies for the identification of treatment failure before they transfer patients from first-line to second-line ART. Participants had clearly articulated that VL testing and CD4 counts assessment are the vital laboratory investigation to be conducted periodically for all patients currently on ART. Participants in the lower level CTC's appreciated the efforts that the government is putting in supplying them with PIMA machine for CD4 assessment, despite frequently stock out of PIMA cartridges. Participants had claimed that they do not have Biochemistry investigations such as the liver functioning test (LFT) and renal functioning test (RFT) and most of the time they refer their patients to private health facilities.

Due to poor supply and availability of viral load, CD4 counts and other potential biochemistry tests in referral municipal hospitals, health centers and dispensaries, clinicians have found difficulty to put their patients on second-line ART. For example, (P19) claimed that he would be comfortable to confirm the first-line treatment failure with CD4 testing and indeed with viral load testing. He suggested that, the government

should critically think of putting viral load machine analyzers to all health facilities providing HIV services countrywide. P10, P13, P21, P26 and P27 openly said that

“After all, the turning around time to get the results back from laboratory of our municipal referral hospital especially CD4 and viral load results takes long times” (P10).

“It is not easy to detect the treatment failure at early stage due to unavailability of CD4 machine and viral load machines at our vicinity”. P13

“I know that we have the point of care (PIMA) machines at health centers CTC to assess patients CD4 counts, then, why can't we have the same point of care viral load machines to assess and easily detect treatment failure for our patients?”

“The need for viral load test makes a big delay in transferring patients into second- line ART” (P26).

“We normally have a panel discussion to discuss on the reasons and agree on the type of second-line drugs that is to be given to patients failing second-line ART however, we are required to prove the failure either through CD4 or viral load testing which we do not have it here” (P27).

P1, P14 and P15 had claimed that, if they had an access to a functional VL, continuous availability CD4 machines and other relevant laboratory tests such as RFT and LFT, their work would have been simple to serve patients in need of second-line, however since there is poor access and availability to VL and CD4 tests, it has been extremely difficult for them to place patients into second-line ART. These participants had specifically pointed out that:

“One of the requirements to shift patients into second line is viral load test. In most of our CTC’s we cannot do it, even here at the regional referral hospital, we do not have the viral load testing facilities and therefore, we normally rely on WHO staging of which I think is not a sorely means for diagnosing first-line treatment failure” (P1).

“Sometimes we sent clients for CD4 testing because our machine is frequently out of order. It is very embarrassing when you have to tell patients to come back for CD4 checks when the machine is ready” (P14).

“We provide service for all patients equally whether they have been referred or they are our daily customers. CD4 machine is free, but other investigations like LFT, and RFT at least they have to pay out of their pocket Eh” (P 15).

availability, accessibility and tolerability to second-line drugs.

The data analysis revealed that second line ART is highly appreciated to HIV patients diagnosed to have first line treatment failure, however the availability, access and sustainability of these drugs are not reliable due to its inadequate supply both in municipal hospitals, health centers and dispensaries. Participants P7, P8, P16, P18 and 23 had amplified that, second-line ART are not readily available and if available are quite expensive and donor dependence in Tanzania. Some participants were free and politely expressed that,

“If patients are diagnosed to have first line ART treatment failure, second-line ARV’s is the only choice we have” (P2).

“.... (Client’s name) was in first line ART and not improving at all, his CD4 was very low. Three months later he was shifted to a second line ART and gradually

improved with no OIs as before. We checked his CD4 which seemed significantly raised. I don't remember exactly how much was the CD4, but it raised. Second line medications are a life-saving to patients failed on first line therapy" (P24).

"We have heard that second line ARV are very expensive hence we might not be able to get them" (P23).

"I believe this is not a political propaganda to tell us to give patients with second line ART, once we decide using them, there should be enough supply and these drugs need to be sustained. We sometimes fail to get enough first line ARVs" (P3).

"We need to have second line drugs and give ourselves to our patients instead of referring them to Temeke hospital" (P30).

"Since we are donor dependency I hope second line drugs will be available... though the government should take charge on these medicines" (P7).

The study revealed that clinicians were enthusiastically willing to prescribe second-line to their patients, however from the knowledge they had in relation to second-line side effects, pill burdens and that, individuals for second-line ART should have adequate supply of food. All these factors, had made clinicians to hastate initiating patients into second-line. While expressing their experience, feelings, fears and worries about the use of second-line ART, some participants stated that;

"Telling the truth, I hate second line ART. I would like patients to only stay on first line ART because of side effects and pill burdens" (P25).

“Aaah, these medications are too much, clients have to swallow them in the morning and evening. Patients claims to have nausea, vomiting, abdominal disturbances and sometimes headache when they take these drugs” (P10).

“My patients complain that, they do not have enough food to take with second line ART. I think second line ART requires patients to have eaten before they swallow them” (P17).

clinicians perceptions on antiretroviral drugs

Findings indicate that participants had negative perception on the future availability of second line ART. Participants depicted that, the country is depending on donors' budget for second line drugs and therefore, there is a chance of having no these drugs in future once the donors pull out to fund the government. They suggested that the government should allocate enough budget for this medication, otherwise there is an alarming imminent shortage of these drugs which in future may cause resistance to these drugs. P2 had viewed that there will be shortage of second-line ART in near future as many patients are expected to be initiated on these medicines. The same conception was declared by P17 who narrated that an intermittent supply of second-line ART would aggravate the existing HIV drugs resistance in the country. Other participants had different thought that;

“If the supply of second-line ARV continue like this, there are chances of having multiple drugs resistance to majority of our patients and the community at large” (P17)

“I think there will be shortage of second line drugs after 5 years since the number of clients will increase” (P20).

“I believe that, there will be stock out of second-line ART as there will be an increase number of clients in need” (P22).

“These medicines are not supposed to be out of stock. Having intermittent supply of these drugs will create and increase ARV resistance to people who misses dosages” (P22).

“I’m too scared, to give second line ART to my patients, if they fail to work what will be the alternative?” (P24).

“I don’t know what will happen if second line ART fails to work to my patients? What will be the next option? Mmh ... I am so much afraid” (P28).

Table 6.

Thematic Area and Categories for RQ2

| Major themes | Categories | Quotes from participants |
|---------------------------|---|--|
| Laboratory investigations | Viral-load and CD4 | It is not easy to detect the treatment |
| | Testing | failure at early stage due to unavailability of CD4 machine and viral load. After all, the turning around time to get the results back for CD4 and V L results takes long times (P13). |
| | WHO eligibility criteria for HIV & AIDS treatment | One of the requirements to shift patients into second line is viral load test. In most of our CTC’s |

table continues

| Major themes | Categories | Quotes from participants |
|--|----------------------------|---|
| ART availability, accessibility and tolerability | | we cannot do it, even here at the regional referral hospital, We do not have the viral load testing facilities and therefore, we normally rely on WHO staging of which I think is not a solely means for diagnosing first-line treatment failure (P1). |
| | ARV medicines side effects | Aaah, these medications are too much, clients have to swallow them in the morning and evening. Patients claims to have nausea, vomiting, abdominal disturbances and sometimes headache when they take these drugs” (P10). |
| | Costs for ART | We have heard that second line ARV are very expensive hence we might not be able to get them (P23). |
| Clinicians perception on ART | Drugs resistance | These medicines are not supposed to be out of stock. Having intermittent supply of these drugs will create and increase ARV resistance to people who |

table continues

| Major themes | Categories | Quotes from participants |
|--------------|------------|--------------------------|
| | | misses dosages (P22). |

patients readiness to antiretroviral drugs.

Participants (P28) had amplified that patients are unaware on the potential benefits on second- line therapy and have misconception on it. Patients are not sure of second-line ART to help them improve health and prolong their life. Some patients are not happy to hear about second-line ART for the rumors that patients taking these drugs have been encountering with multiple complications such as severe diarrheas and vomiting. Nevertheless, second-line ART are perceived to be the last options drugs for HIV treatment among PLHIV. This notion was stated by few participants who actually outlined that;

“My patients are very worried to be switched into second line ARVs. They keep on asking me if they will stay safe with second-line treatment or does the second-line treatment implies end of their life.” (P29).

“We had two patients who refused to go to Temeke municipal referral hospital after we had told them that, they will need to switch into second line ARV medications which we don’t have them at our CTC” (P25).

Participants (P3, P7, P13, P15, P20, P23 and P26) had explained that patients are sometimes resistant when informed about the shift of one regime to another. It is a normal habit to hear patients refusing being transferred into second-line ART plan. This

phenomenon occurs only when there is an asymmetrical information about ARV medication, between patients and health care providers at CTC. P23 gave his experience of attending several angry patients who do not prefer and are not ready to be shifted into second-line ART. He recommended that patients should be made aware and provided with full information about their treatment before any anticipated treatment change. To comment on the point as above, P28 clearly narrated that;

“Patients feels OK if given adherence counseling and education on why they should be switched to second line ARVs” (P28).

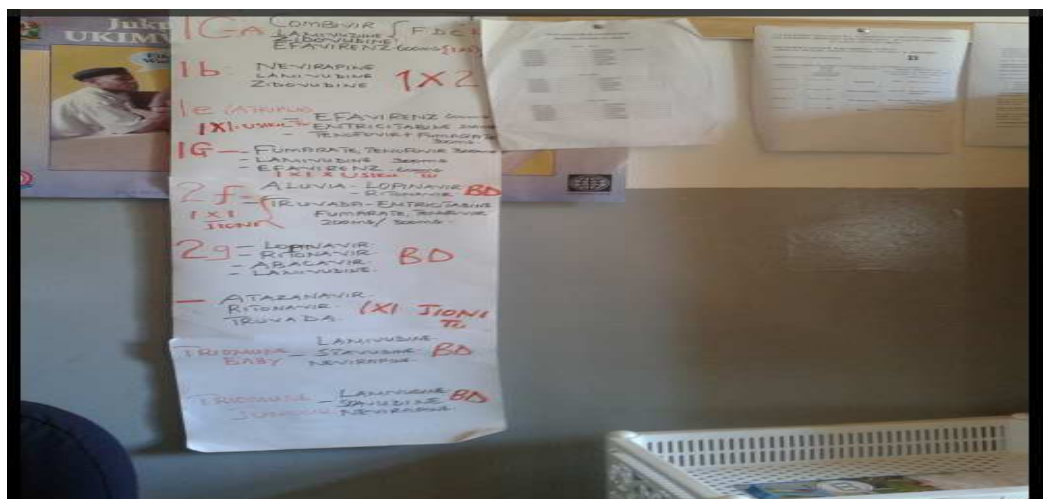


Figure 1. Types of second-line ART.

adherence and retention to antiretroviral drugs.

Findings indicated that with proper adherence counselling, HIV patients would warmly welcome and accept second line ART. Participants emphasized on the need for continuous supportive counselling both for the family members and the individual patients. Failure to do so, majority of their patients stops treatment and may throw out drugs onto dust bins.



Figure 2. Patient throwing second-line ART.

P6, P9 and P10 emphasized that there should be a continuous and supportive adherence counselling for people on ART medication in order to reduce issues on lost to follow up, drug resistance, morbidity and mortality among HIV patients. In relation to ART medication adherence, some participants had clarified that;

“At first there were problem with adherence, but later they adhere very well” (P14).

“Adherence counselling makes patients to be very serious and stick to their medications” (P1).

“Aaah Mmh ... If the treatment failure is due to first line poor adherence, I also predict poor adherence to patients who will be switched to second- line ART (P19).

“If relatives are not properly counselled and made aware on the medications changes, they will not allow their relatives to take second line ART and therefore they will be poor treatment adherence” (P15).

“Once relatives of the patient are educated on second line ART, they usually accept the treatment and support their patients to take medications” (P27).

“If relatives are forced to let their patients take second-line medications without their consent, these patients will stop taking drugs and throw them in dust bins” (P8)

Table 7.

Thematic Area and Categories for RQ3

| Major themes | Categories | Quotes from participants |
|--------------------------------|-------------------------------|--|
| Readiness to second-line ART | ART readiness | We had two patients who refused to go to the Temeke municipal hospital after we had told them that, they will need to switch into second line ARV medications which we don't have them at our CTC (P25). |
| Adherence and retention to ART | Supportive counseling for ART | Aaah Mmh ... If the treatment failure is due to first-line poor adherence, I also predict poor adherence to patients who will be switched to second line ART (P19). |

Summary

This chapter includes six thematic analysis areas. Of these themes one was derived from RQ1, three themes from RQ2 and two themes were from RQ3. Data for analysis were obtained from the electronic transcribed documents that had raw data

collected from clinicians working in Dar es Salaam HIV CTC's. Analysis was done through the aid of atlas.ti.7.1.3. The chapter had illustrated findings to reflect the research questions of the researched topic. The next chapter includes sections for discussion, conclusion, and recommendations.

Chapter 5: Discussion, Conclusion and Recommendations

Introduction

The chapter begins by providing concisely summary that reiterate ideas, nature of the exploration and the reason as to why it was conducted. The summary of findings

including barriers of clinicians for delaying transferring of patients from first- line to second-line ART has been amplified in the next section of this chapter. The next chapter shows interpretation of findings in relation to literature review and the conceptual theoretical framework. The next section of this chapter includes limitations to trustworthiness that arose from execution of the study. The next section of the chapter includes recommendations for further research while utilizing the strengths and limitations identified in this study and other studies in the literature review. The next section of the chapter includes practical implications and positive social change that have been identified from this study. The final section of this chapter provide conclusion that shows the key essence of this research.

Nature of the Study

I applied a descriptive qualitative research design (Aschengrau & Seage, 2014), to explore innovative strategies that will remain to solve the dilemmas that impacts clinician decisions of not switching patients on second line ART. This study had applied PAR approach (Yin, 2014). To my best knowledge, there is no research that has been done through PAR theoretical framework to assess clinician's perceptions and experiences on transferring patients into second-line ART particularly in Tanzania.

The purpose of this study was to discover barriers of clinicians for delaying transfer of individuals from first-line to second-line ARV therapy in Tanzania. Switching percentages of patients to second-line ART is a challenge in Tanzania (Ramadhan et al., 2014). Little information currently exists about the predictors of first-line and second-line treatment failure among patients in HIV programs (NACP, 2012). A recent study

conducted in Tanzania indicated a resistance level of 14.8% to first-line ART patients (Kasang et al., 2012). Thus, one must ask why clinicians are not transferring these patients into second-line therapy. The barriers that prevent clinicians from transferring patients to second-line ART have not been explored. Because PAR approach helps researchers to work together with participants, I used this approach to explore barriers that may be influencing clinicians' decisions to transferring their patients into second-line ART. To address the research topic I used the following research questions:

RQ1: What factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

RQ2: What are clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

RQ3: What factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

The study population was clinicians working at CTCs from the three Dar es Salaam municipalities (Kinondoni, Ilala and Temeke municipalities).

Key Findings

Based on the shared views from clinicians who participated in the study, findings identified that clinicians have low knowledge, competence and experience on the WHO second-line treatment criteria, second-line ART switching timing as well the history taking to detect first-line treatment failure. All these factors causes delays in switching

patients into second-line therapy. Lack of laboratory investigations such as viral load and CD4 testing are the major factors hindering clinician's determination of making decision to transfer their patients into second-line therapy. As such, participants had perceived that the government depends much on donor funded ARV procurement which in future may lead poor availability and access to second-line ART and hence creating drug resistance.

Nevertheless, even at the movement clinicians have eluded that there is intermittent supply of second-line ARV which are then believed to have a lot of side effects. Due to poor supply and side effects associated with second-line ART, participants finds difficult initiates their patients into these drugs. Findings also revealed that, participants would only initiate second-line ART to patients who had good adherence to first-line ART to whom it has failed. Patients to be switched into second-line ART must as well be fully counselled and ready to take these drugs. In the case that patients had poor adherence to first-line ART and not ready to start second-line, participants failed to have the decision to switch them into other options such as second-line ART.

Interpretation of the Findings Per Research Questions

RQ1: what factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

Based on explanations from participants who participated in the study, this research identified three frequent factors that influence clinicians' decision to switch

patients from first line to second-line ART, these factors include low knowledge, competence, experience and switching timeline for second -line ART. These findings concur with Barnett et al. (2013), who concluded that clinicians' knowledge and competence is essential to the timely switch of HIV patients to second-line ART. Without adequate knowledge, clinicians may lack the confidence to adjust patients' treatment plans when needed (Ramadhan et al., 2014). Inadequate capacity to diagnose first-line treatment failure causes delays in switching them into second-line therapy in Tanzania and other Sub-Saharan countries. For example, during their study in Mozambique and Uganda (Costenaro et al., 2014) found that reduced capacity to monitor and detect the failure of first-line ART was a key reason that clinicians delayed switching patients to second-line therapy.

Findings reveals that participants had inadequate knowledge and were not competent at taking history and examining patients to establish first-line treatment failure and the need for switching them into second-line ART. History taking and patients examinations should has been seen as a pivot for assessing PLHIV during ART refilling and other medications when patients attends their scheduled visits at CTC . Clinicians should regularly take history and physical examination to their patients in order to evaluate appearance or persistence of opportunistic infections, or lack of weight gain that may be a good indicator for patients treatment failure (Laurent et al., 2012), which necessitate the use of second-line ART (Aberg et al., 2014).

Clinicians should maintain a culture of performing both physical and systematic examination for their patients during each visit at care and treatment health facilities.

This will facilitate and help them detect early symptoms of first-line treatment failure. Nevertheless, clinicians should also keep in mind that clinical criteria alone do not guarantee switching of individuals into second-line ART, however, other switching parameters need to be considered as well. Findings show that participants had poor experience on when was the appropriate time for switching their patients into second-line ART. The time elapsed from first-line treatment failure to switching patients into second-line greatly varied among participants.

At least 10 out of 30 participants did not have any idea on when is the appropriate time to transfer patients into second-line ART. Five out of 30 had said that, they would switch their patients into second-line ART two weeks after they had failed first-line ART. Four out of 30 participants would shift their patients into second-line ART one week after they had failed first-line ART. Three participants mentioned to be switching their patients into second-line one month after they have failed first-line, two participants had said to have transferred their patients into second-line three months later after they had failed first-line ART (Table 5).

Other two participants had said that, they would switch their patients into second-line ART 6 months later. Where two participants would transfer patients one year later after a failure of first-line. One participant would transfer his patients to second-line one and half year when first-line is confirmed to have failed. One participant concluded that he would switch her/his patients to a second-line ART two years later (Table 5). This indicates that, there is unclear timing of when to switching patients into second-line ART. If this remain uncontrolled there are possibilities of having people with multiple

drugs resistance for ART including the second-line options. This is a novel finding that has not yet been posited in any literature reviews demonstrated in chapter 2 of this study and that need great attention.

Findings from this study eluded that though participants had seen the importance of using laboratory investigations such as viral load testing and CD4 counts for making decision in transferring their patients into second line ARVs. Lack of Biochemistry investigations such as the liver functioning test (LFT) and renal functioning test (RFT) still a challenge because these investigations are accessed through private health facilities where patients are usually referred for. Participants in the lower level of CTC's appreciates the efforts that the government is putting in supplying them with PIMA machine for CD4 assessments, despite frequently stock out of PIMA cartilages and other reagents.

Due to lack of viral load testing, inadequate supply and availability of CD4 assessments and other potential biochemistry tests in CTC's, clinicians relies on clinical WHO criteria to detect first-line treatment failure, which often results in poor treatment outcomes and drug resistance (Bacha et al., 2012; Robert et al., 2012), and therefore, progression of HIV to AIDS related illness and complications. Study findings correlate with those from Ramadhan et al., (2014), who also found that, poor access to laboratory tests contributes to in-effective HIV treatment in most Sub-Saharan nations in Africa. According to Adeyinka & Ogunniyi (2012), viral load monitoring is inaccessible to many clinicians in this region.

Therefore, the lack of viral load monitoring, CD4 test, LFT and RFT if not well addressed will continue to create lower than expected rates of switching patients into second-line ART regimens in resource-limited settings including Tanzania. It is no doubt that, the use of viral load in particular, will reduce shift of patients from first-line to expensive and non-tolerated second-line therapy as many of them will be identified early before they fail the first-line ART. In this study, findings shows that second-line ART is highly appreciated among clinicians working at CTC and they all recommend that HIV patients diagnosed to have first- line treatment failure should be switched to second-line ART in order to improve their health.

This finding confers with the WHO statement that state that, second-line ART should be given when first-line ART has been proven to have failed to suppress an individual HIV virus replication in the human body (WHO, 2013a). All patient deteriorating on first-line ART can benefit from second-line therapy, keeping them on first-line therapy will not help them reduce their viral loads and improve CD4 counts (WHO, 2014). Despite the WHO statement, many patients are not transferred into second-line in most of the CTC's in Dar es Salaam region. This finding relates to those found in South African and Asian studies, where clinicians perceived that second-line HIV medicines were expensive (Meintjes et al., 2014).

The prices of second-line have remained higher than for first-line regimens (Estill et al., 2016). The pricing evidence has been observed from a South African study that revealed that the cost of second-line treatment doubles first-line ART price in a year (WHO, 2013b). It is anticipated that the use of second-line ART will increase in the near

future due increase of patients needing second-line ART (Long et al., 2012), while prices for second-line ART are non-predictable for patients to afford (Ramadhan et al., 2014). As from these reasons, there is no doubt that clinicians will continue delaying switching their patients into second-line ART.

RQ2: what are clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

Findings revealed that clinicians are enthusiastically willing to prescribe second-line ART to their patients, however from the knowledge that clinicians have in relation to second-line ART, participants eluded that second-line ART is associated with a lot of side effects, pill burdens and that, individuals taking second-line ART should have adequate supply of food during the entire course of drugs medication. All these factors, had made clinicians to hastate putting patients into second-line. My findings bridge on other findings from researchers (Barnett, 2013; Sahay, Reddy, & Dhayarkar, 2012) who reported that barriers to second-line ART included side-effects, regimen complexity, socio-cultural factors such as complex dosing schedules, alcohol, and substance abuse. Ramadhan et al. (2014, p. 2) reported that distance from HIV care and treatment clinics, economic factors, and patient-provider relationships may also contribute to patients delays in switching to second-line ART.

Meintjes et al. (2012) reported that medication used in second-line ART is rarely tolerated by patients, due to toxicity such as hypersensitivity reaction; kidney failure; progressive neuropathy and gastrointestinal complaints. Toxicities due to medication

often prompts poor second-line ART uptakes among PLHIV (Ciaffi et al., 2015).

Finding revealed that often, clinicians working in CTC do not trust WHO criteria for diagnosing and detecting ART treatment needs due to the poor reliability of clinical and immunological assessments (Ramadhan et al., 2014). Clinicians' skepticisms of WHO criteria contribute to the low number of patients switched to second-line ART (Vanobberghen, 2015).

Participants in this study had noted that, they would like to switch their patients into second-line ART, but they are not sure on the second-line treatment safety and therefore they remain reticent to switch patients to second-line ART, despite poor clinical prognosis they observe from their patients. Even when patients are aware of ART goals, clinicians continued to hesitate in placing patients on appropriate ART for a number of reasons, such as (a) ART toxicity, (b) issues related to quality of life, and (c) fears of long-term adverse drug reactions. It is therefore recommended that clinicians prescribe ART that is best at delaying viral replication, delaying illness development, and improving quality of life for patients (WHO, 2013b). There should be a mutual relationship between clinicians and patients to decide when to start ART. Both advantages and disadvantages of using ART be discussed and agreed upon between clinicians and patients.

In this study, there was no any participant that had mentioned issues on ARV drug interactions, this could be attributed by the fact that, clinicians may not have adequate knowledge about drug interaction as mentioned in the literature review- chapter 2. In this study participants appeared to have a negative perception on the future availability of

second-line ART. Participants had explained that, the country is highly donor dependent and does not have adequate budget for second-line ARV and therefore, there are likelihood of stock out to these drugs in the near future and especially when donor agencies pulls out to funding the government. They suggested that the government of Tanzania should allocate enough budget for this medication.

These findings concurs with those articulated by Chkhartishvili et al. (2014) and Johnston et al. (2012) who said that, an increased number of patients experiencing first-line treatment failure, will grant many patients to be shifted into more expensive second-line ART (Bacha, Tilahun, & Worku, 2012), and the development of viral resistance (Ramadhan et al., 2014). Inadequate availability, access and, or supply of second-line ART in Tanzania, calls for political will and more budget allocation to prioritize on these drugs.

RQ3: what factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

In this study clinicians, have amplified that patients are unaware on the potential benefits of second-line ART. Some patients had a positive attitude toward the second-line treatment knowing that this treatment will help them to improve health and prolong their life. Others were not happy for such information and were not ready to shift into second-line ART. Indeed, Patients' readiness for antiretroviral use was a common mentioned enabler to influence clinicians to easily initiates patients into second-line ART. Patients' readiness to second-line ARVs has been found to be a strong enabler for clinicians to switching clients to the required treatment. It is therefore the duty of

clinicians to prepare patients before they initiate them into ARV medicines and in particular to second ART. Findings of this study clearly showed that HIV patients would warmly welcome and accept second-line ART if proper adherence counseling were to be conducted to them.

Participants had emphasized on the need for continuous supportive counselling both for the family members and the individual patients. Failure to do so, majority of patients will often stop ART treatment. Inadequate patient counseling can result in poor treatment adherence (South Africa Department of Health, 2014) and patients transferred to second-line ART due to first-line nonadherence are less likely to attain viral suppression (Murphy et al., 2012) because second-line treatment success depends on first-line adherence practices (Keiser, et al., 2012). This observation suggests that medication nonadherence is responsible for treatment failure among patients switched into second-line ART (Hansana et al., 2013). Because success of second-line ART depends on high levels of adherence, these observations imply that adherence on first-line may be an important indicator of adherence to second-line ART (Murphy et al., 2012).

Adherence to ART means sticking firmly to treatment regimen by taking HIV medicines every day and exactly as agreed between clinician, client and treatment supporter, in case of minors (Hansana et al., 2013). Adherence has been correlated strongly with HIV viral suppression, reduced rates of resistance, an increase in survival, improved quality of life and prevent the spread of HIV to partners and offspring (CDC, 2016). Adherence to ARV's medication is a critical aspect for HIV treatment success (WHO, 2016). And it is required at a rate of >95% to maximize the benefits of ART

(Murphy et al., 2012). Because it is difficult to maintain such rates, Odendal (2014), has advised that HIV programs across the world should use continuous and supportive adherence counselling for people on ART medication.

Efforts should be made toward suppression of an individual's HIV in the body than curing AIDS (Hansana et al., 2013). As such, attaining the required level of ARV drug adherence is important because viral suppression cannot be achieved when ARV drugs are not used as prescribed, and for life (Ciaffi et al., 2015). And that, poor ARV medication causes transmutations of the virus and later drugs resistant (Carter, 2012). Findings from Uganda study revealed that improper adherence to ART leads to poor suppression of HIV replication of individual infected cells and therefore increasing prevalence of HIV in the community (Buyu et al., 2016). Lack of ART adherence, promotes transmission of drug resistant HIV among individuals in the community (Schaecher, 2013).

Drug resistance causes first- line treatment failure (Levison et al., 2012). Adherence should be considered as an important aspect for successful HIV treatment. Previous studies denote that the risk of emergence of drug resistance with suboptimal adherence is generally greater in patients taking NNRTIs compared with most PIs (Carter, 2012), and that adherence was improved in subjects randomized to switch from a PI to EFV or to ABC compared with those who continued the PI based regimen (Van Zyl et al., 2012). Other investigators have reported improvements in quality of life, as assessed by questionnaires, in two randomized studies in which PI's were switched to NVP or to either NVP or EFV compared with continuing the PI (CDC, 2014).

Theoretical Framework

In my study, I used PRA to establish and describes barriers of clinicians for delaying transferring of their patients from first line to second-line ARV therapy in adults' HIV patients. To my knowledge, my study is the first one to use PAR to inquires clinicians' reasons of not transferring individuals' patients into second-line therapy in Tanzania. PRA has been defined as a research approach that involves the active participation of stakeholders whose lives are affected by the issue being studied in all phases of research to produce constructive changes into that community (Chevalier & Buckles, 2013). PRA is collaborative in nature because the researchers and participants identify the problem together. The participants and the researcher learn from each other and understand one another's perspectives (Stoto, Nelson, & Klaiman, 2012).

PRA approach allows the researchers to work together with those affected in finding solutions to their problem. The researcher also classifies data into themes and performs analysis to describe its meanings (Stoto et al., 2012). While using PRA in this study, I was able to explore feelings and perceptions of clinicians who delays transferring patients from first-line to second-line ART in order to improve HIV care and treatment services in Tanzania. Various qualitative studies using the PAR approach have also been done to explore the perceptions and feelings of PLHIV on the ART uptake. In Kenya for example, Otieno, Obondo, and Mathai (2012) used PAR to investigate factors influencing non-adherence of ART to patients in relation to alcohol abuse. With PAR approach both clinicians and patients were able to communicate the importance of ART and identified the associated risks of alcohol consumption and the use of ART.

Evidence shows that PAR is a good approach in improving HIV treatment adherence and preventing treatment failure and drug resistance to PLHIV (Tangpukdee, 2012). With PAR, I engaged clinicians to find out factors influencing them at shifting patients from first-line to second-line ART in Tanzania. I used PAR to make sense of the data and help me to explore the use of second-line therapy among PLHIV. Richter et al. (2015) confirmed use of PAR in six countries Canada, Jamaica, Barbados, Kenya, Uganda and South Africa to empower nurses and other health professional to make decision that intended to improve health systems for HIV and AIDS nursing care. As with my study, PAR has been used to empower clinicians to establish barriers that makes them to delay in transferring their patients into second-line ART.

PAR was useful to promote clinicians to be free and being able to express themselves on the reasons, perceptions and facilitating factors that can influence their decision making when trying to shift their patients into second-line ART. Nevertheless, in collaboration with participants, I prepared a simple action plan to each individual CTC in order to help the individual participants to maximize this study recommendations into practice.

Limitations of the Study

Limitations are inherent to the research. Due to financial constraints, this study was limited to clinicians working in Dar es Salaam city-HIV CTC's alone. Findings in this research may not be generalized to other populations but its practical recommendations can be adopted elsewhere in sites implementing HIV and AIDS care in the country and globally. Further, this study did not include laboratory personnel and,

therefore, some information relating to the switching of patients to second-line ART may have been missed from this group of experts. Laboratory personnel were purposively excluded in the study for the reason that, they neither not prescribe nor provide ARV medication adherence to PLHIV but performs laboratory investigation alone and reports it to clinicians who further decides medications for patients. Data were only limited to individual interview questions that matches with PAR and for that matter, some participants may have not provided all possible details.

Although many children in Tanzania are infected with HIV, results of this study intended to study clinicians who only work with adult patients in order to easily explore causes for delaying switching patients into second-line ART. Previous literature review in chapter 2 depicted that, stressed/burnout implicated to clinicians may explain the reason as to why clinicians' delays transferring of patients into second-line ART. My findings in this study did not explored issues for discussion on stress/burnout among clinicians and therefore, this was not considered as a thematic area for analysis in this study.

Recommendations for Practice and Future Research

The most important issue here is for the policy makers in the government and other HIV implementing stakeholders in Tanzania to strengthen health system through enhancement of laboratory investigations (Viral load, CD4 and Biochemistry testing) and making them available in all CTC's in the country. Tanzania may need to widening adequate supply of second-line ART into all lower level of CTC's and making it available and accessible. The Ministry of health and other stakeholders in Tanzania

should conduct capacity building among clinicians in order to equip them with proper skills that will facilitate quick decision making for switching HIV patients into second-line therapy. This capacity building could be done through a formal and scheduled HIV management related trainings, regular supportive supervisions to CTC's, regular mentorships to CTC's, sharing of WHO HIV related updates and information via individuals local and international meetings, seminars, workshops, symposiums, webinars and teleconferences.

Municipals/regions, district councils and individuals CTC's can be reinforced with updated HIV and AIDS policies, guidelines, strategies, standard operating manuals, treatment protocols, recording and reporting tools that will make them accountable in rendering HIV care in their jurisdictions. Regional and Council Health Management Teams should see the need to in-cooperate HIV care and treatment trainings into their annual budgets in order to able scaling of trainings related to HIV knowledge to the lower levels of HIV implementation and in particular to clinicians working into CTC's. The government of Tanzania should wave from the donor dependence on the procurement of both first-line and second-line ART and, thus, the government should allocate enough funds for the sake of maintaining continuous supply of ARV across all CTC's in the country.

The government of Tanzania should use findings of this study to communicate with all HIV health facilities in order to reduce barriers that have been seen to hinder clinicians' decision making for transferring patients into second-line ART to PLHIV. The government should create and share any WHO updated knowledge to clinicians on

how to identify first-line treatment failure to HIV patients and ultimately switching them into appropriate required regimens. It is the duty of the government of Tanzania to acknowledge this unpleasant culture and creates participation, responsibility, commitment strategy and designing good working environment that will influence clinician's determination to transfer patients into second-line ART and therefore improving quality of HIV care and treatment among PLHIV.

Further study is required to explore reasons for delaying switching children into second-line ART. Studies should further be conducted to explore if whether stressed/burnout influences clinicians' decision making to transfer patients into second-line in Tanzania. A mixed study (Quantitative-Survey and Qualitative study) could be important to complement findings of this study.

Implications

Positive social change

Study findings may inform HIV planners, policy and decision makers, HIV program managers and CTC's managers, researchers, health monitoring and evaluation specialists, program developers and clinicians on specific strategies to improve HIV care and treatment across all CTC's in Tanzania. My findings generate knowledge to help clinicians to easily identify HIV patients who are in need of a second-line ART. Through meetings, workshops, seminars, local and international conferences, symposium and webinars, this finding will be used to improve clinical health care services in the community, rather than seeking individuals or health system accountability in rendering HIV care.

Through journal, articles and bulletins findings of this research will inform policymakers on the need to provide clinicians with training to help them make proper decisions on when to switch HIV patients to second-line therapy. Through use of my study recommendations, the government and other HIV implementing stakeholders in Tanzania should develop strategies to promote treatment with second-line ART for patients deteriorating on first-line therapy. According to Tangpukdee (2012), PAR theoretical framework is the best approach for health problems solving in the community and can be used to other areas of public health leave alone the HIV condition as stipulated in this study.

PAR is appropriate for descriptive qualitative study designs that may help researchers to explore individuals, and or communities' insights, experiences and perceptions about a specific phenomenon (Bradley, Lehmann, & Butler, 2015). The methodology used in this study can also be applied else for findings transferability.

Conclusion

Global initiatives on HIV management emphasize much on the long-term difficulties of managing HIV and AIDS and not on the short-term benefits of ART such as suppressing individuals' HIV in the body, restoring immunity and preventing death among PLHIV but rather controlling the outcomes that may be associated with the long-term use of ART as well as improving quality adjusted life years (QALY) and disability adjusted life years (DALY) for PLHIV (Keiser et al., 2012). The idea of transferring HIV patients diagnosed to have first-line treatment failure to second-line ART is of great

important, because keeping them on first-line therapy will not help them reduce their viral loads and improve CD4 counts (WHO, 2014).

Several HIV initiatives have been introduced to a great number of African countries in attempt to providing free ART to its people infected with HIV (Sidibé, Zuniga, & Montaner, 2014). However, the scaling up of this initiative is still a big challenge in these countries because countries that have access to ART such as Tanzania, clinicians often fail to switch patients from initial first-line ART to subsequent second-line ART when first-line treatments lose effectiveness (Ramadhan et al., 2014). The existing culture of clinicians of not switching patients into second-line in Tanzania has been built upon since the inception of HIV care and treatment program in the country in 2005, and actually this could be referred as a negative construct of its own reality (Ramadhan et al., 2014).

One may argue that the observed negative culture among clinicians is due to the existing weakness of the health system in Tanzania where clinicians are not well-trained and have poor capacity to diagnosed first-line treatment failure. This culture could be a result of inadequate supply of laboratory investigations such as viral load and CD4 test in CTC's to explain the reason as to why clinicians delays in making decision to transferring patients into second-line ART. It could also be due to perceptions that clinicians have on the availability, access, and tolerability of second-line ART. For that matter, they hesitate to shift their patients into second-line ART. Additionally, it could be that patient's readiness and adherence to second-line ART may promote clinicians' initiatives to transfer patients into second-line ART.

There are no proper answers for the questions asked above, however, it may be important for the government of Tanzania to transform these negative cultures into a positive value. It is the duty of the government of Tanzania to acknowledge the observed culture and creates participation, responsibility, commitment strategy and designing a good working environment that will influence clinician's decision to transfer patients into second-line ART and therefore improving quality of HIV care and treatment among PLHIV in the country (Kasanga et al., 2012).

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Appendix A. Interview Protocol

Topic: Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania

Introduction

Date: __/__/____ [DD/MM/YYYY]

Participants Information

Participant ID number: -----

Participant's initials: -----

Region:.....

Health Facility Name: -----

Qualifications:.....

RQ1. What factors influence clinicians' decisions to transfer adult HIV patients from first-line to second-line ART in HIV facilities of Dar es Salaam region?

1. Describe your experience in working in HIV care and treatment clinics
2. Can you describe the WHO recommended stages of HIV disease?
3. Can you describe the antiretroviral drugs used in management of HIV?
4. What factors would you consider to establish before initiation of ART to PLHV?
5. Can you narrate factors that may influence clinicians to switch a patient from first to second line antiretroviral therapy?
6. At what point would you consider switching patients from first to second line ART

7. Can you describe the necessary steps one should follow before switching patients to second line antiretroviral therapy and how does this affect the switching process?
8. Describe the side effects of second line antiretroviral drugs if any?
9. Can you narrate the advantages of switching the patients to second line antiretroviral therapy?

RQ2. What are the clinicians' perceived barriers and understandings regarding switching HIV individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

1. Describe the barriers one may encounter when trying to switch a patient to second line antiretroviral therapy
2. How do you feel about switching patients to second line antiretroviral therapy when there is a need to do so?
3. What is your opinion on second line antiretroviral therapy?
4. Explain if you have any fear or belief at switching patients into second line antiretroviral therapy
5. What are your opinions of second line ART against other alternative medicines?
6. During your life experience in working at CTC, you may have encountered with stress or burnout. How would you describe this?
7. Have you ever heard about viral load and immunological test, what does these terms implies?
8. Are there any advantages or disadvantage of using viral load and immunological test to PLHIV?

9. What is your opinion on the access and availability of viral load and immunological test in relation to switching patients into second line antiretroviral therapy in your facility?
10. Can you explain the time that it takes from diagnosis of treatment failure to switching to second line antiretroviral therapy?
11. What are your thought in relation to access and availability of second line antiretroviral therapy at your facility?
12. What is opinion on the long term sustainability of second line antiretroviral therapy drug supply?

RQ3:What factors may enable clinicians to switch individuals from first- to second-line ART in HIV facilities of Dar es Salaam region?

1. What are the enabling factors that if given to you can influence and improve your decision of transferring patients from first to second- line ART?
2. Explain the side effects and tolerability that may be associated with second line ART?
3. How do your patients react when you tell them that they are supposed to be switched to second line?
4. What is the readiness of patients prepared when you tell them about switching them to second line antiretroviral therapy?
5. How do their treatment supporters/ family react when you tell them that their relatives are supposed to be switched on second line antiretroviral therapy?
6. Explain how patients and their families react and feels when they are told about second line antiretroviral therapy switching.
7. How would you describe ART adherence in regards to treatment services as well second line switching

8. How would describe the clinical criteria at initiating second line ART?

Appendix B. Recruitment Flyer

**VOLUNTEERS WANTED FOR A RESEARCH STUDY**

Study Title: *“Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania”.*

Are you over the age of 18 and currently working in HIV care and Treatment Clinic and having at least 12 months working experience in provision of ART to people living with HIV and AIDS? I’m conducting a research study about Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania and looking for your input. The intention of this research is to establish barriers that are related to clinicians for delaying switching HIV individuals into second-line antiretroviral therapy, and without considering the emerging resistance to first-line antiretroviral therapy

Procedures:

Assenting to participate in this research, will require to:

- Take part 30-45 minutes a face to face interview.
- Describes barriers and experiences that influences your decision making at transferring people from first-line to second-line ART
- Permit interview to be audio-taped. You can refuse to be recorded, but recording the interview will allow the researcher an opportunity to review your responses in-depth.

- Meet with the researcher a second time to review the interpretation of findings to confirm that the researcher has captured an accurate account of the barriers and experiences that influence decision making at shifting patients from second line ART. You can decline the additional meeting with no repercussions and it will not impact initial interview.

Benefits and Risks:

While participating in this research, you may experience a bit of risk which are actually minor to subject you into discomforts. Some of these discomforts may include fatigue and stress. It is my hope that this study will not subject you to any risk or threats your health. In case of any discomforts you can decline to respond whichever inquiry or terminate the interrogation at any moment in time

Payment:

Assenting to participate in this research will let you will receive a 10,000 T.sh for your engagement at the end of the interrogation .

Privacy:

I will keep confidential any of the information you provided to me. I will not utilize your particulars either in any presentation or publications. The data you provide to me will be protected and secured under the following data management plan:

- Every opportunity will be taken to ensure personal information is secure.
- Audio recorded information's will merely be listened and transcribed by an investigator. All paper records will strictly be secured and protected in a safe files cabinet

- All electronic files will have password to protect them from illegal authorization other than the investigator.
- All identifying information will be removed from written records and pseudonyms will be utilized in the transcripts and final report.
- I will keep your data for 5 years as per the university requirement.

Study contacts:

This research is conducted under the direction of Dr. Patrick Tschida, the Dissertation Chair who can be reached through a phone no. xxxx or an email xxx. The study it has the IRB approval number is 08- 29-16-0309530 which expires on August 28, 2017. Should you need further clarifications about the study, let me know through my mobile no. xxx or through an email xxx. You may also reach Dr. Leilani Endicott a University member to query this study. Use this number xxx to call her.

Appendix C. Recruitment Email-Script

Greetings

My name is xxx, a researcher and a Walden University doctoral student . I'm carrying out a study on the "Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania". I am emailing to ask if you would like to take part to an interview of about 30-45 minutes for this research project. Participation is completely voluntary and your answers will be anonymous.

If you are interested, please respond in this email xxx

This research is conducted under the direction of Dr. Patrick Tschida, the Dissertation Chair who can be reached through a phone no. xxx or an email xxx. The study it has the IRB approval number is 08- 29-16-0309530 which expires on August 28, 2017. Should you need further clarifications about the study, let me know through my mobile no. xxx or through an email xxx. You may also reach Dr. Leilani Endicott a Univesity member to query this study. Use this number xxx to call her.

Thank you for your time.

Signed: xxxxxx

PhD student

Walden University

Appendix D. A Phone Recruitment Script

Hellow my name is xxxx, a researcher and a Walden University doctoral student . I'm carrying a study on the "Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania". I am calling to ask if you would be willing to let me interview you. It should take about 30-45 minutes to complete the interview and participation is completely voluntary and your answers will be anonymous.

If you would be interested in participating in this interview, we can set up a time now or you can let me know when a good time would be to schedule it and if you are not interested, let me know please!

I can be reached at xxx or through an email xxx. Thank you for your help.

Appendix E. Permission Letter

WALDEN UNIVERSITY*A higher degree. A higher purpose.*

xxx Washington Avenue South, Suite XXX
 Minneapolis, Minnesota xxx. Admissions Office XXX South Exeter Street
 Baltimore, Maryland xxx

Municipal Medical Officer of Health
 xxx Municipal Council
 P.O.Box xxx,
 Dar es Salaam,
 15th July 2016.

RE: A Request to Conduct a Research

Dear Sir/Madam

I am writing to inquire an authorization to carry out a research study at your municipal. I am a Walden University doctoral student and I'm in the process of carrying a study on the "Barriers of Clinicians in Switching Patients on Second- line Antiretroviral Therapy in Tanzania" as part of my dissertation.

I trust that the municipal management will let me engage (2 clinicians from xxx referral hospital- care and treatment clinic, 2 clinicians from urban health centre with HIV care and treatment clinic, 2 clinician from rural health centre with HIV care and treatment clinic, 2 clinicians from urban dispensary with HIV care and treatment clinic and 2 clinicians from rural dispensary with HIV care and treatment clinic) to anonymously take part to an interview of about 30-45 minutes in this research project.

Volunteering clinicians in this study will be provided with a written consent form to sign for their acceptance to participate in the study. Clinicians who volunteer to participate will also be given a signed copy of the consent form to remain with it. Upon your permission, agreeing clinicians will meet the researcher for interview at a location and time that is convenient to participants. Interview locations will be quiet and free from distractions.

Once the research is over, I undertake to provide your institutions with a bound copy of the full research report. There is no payment that is required from you, health facilities and the clinicians who will participate in this study.

Your endorsement to carry out this research will deeply be esteemed. I will call you next week for follow-up and in the case of any concerns about this research let me know

please so that I provide further clarifications. Please feel free to reach me both at my email xxx and mobile-phone no. xxx.

If satisfied with these explanations, ; I humbly request you to sign below and remit the endorsed letter to me. Should you have any alternative of allowing me to conduct this study, again let me know please.

Sincerely,
xxxx,

Walden University Student

Approved by:

Print your name and title here

Signature

Date